Platelet Abnormalities in the Oral Maxillofacial Surgery Patient

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KEYWORDS

• Platelets • Immune-mediated thrombocytopenias • Drug-induced thrombocytopenias
• Congenital thrombocytopenias • Acquired thrombocytopenias • Thrombocytosis

KEY POINTS

- Platelet abnormalities result from a wide range of congenital and acquired conditions, which may be known or unknown to patients presenting for oral maxillofacial surgery.
- It is critical to obtain a thorough history, including discussion of any episodes of bleeding or easy bruising, to potentially discern patients with an underlying platelet disorder.
- If patients indicate a positive history, preoperative laboratory studies are indicated, with potential referral or consultation with a hematologist.
- Appropriate preoperative planning may reduce the risk of bleeding associated with platelet dysfunction, potentially avoiding serious perioperative and postoperative complications.

INTRODUCTION

Platelets have multiple functions involving a complex spectrum of processes from hemostasis to thrombosis. Platelet abnormalities have a multifactorial cause when encountered in patients presenting for oral and maxillofacial surgery in both the inpatient and the outpatient environments. It is essential to have an understanding of the physiologic mechanisms underlying platelet disorders in order to effectively manage patients and reduce potential surgical complications within this heterogeneous population. This article provides an overview of platelet physiology and platelet dysfunction, including thrombocytopenia and thrombocytosis.

PHYSIOLOGY OF NORMAL PLATELETS

Platelets are small, nonnucleated cells derived from precursor proplatelets produced by megakaryocytes found in bone marrow. A normal platelet concentration within the blood is between 150,000 and 450,000 cells per microliter. The typical duration of platelet circulation within the human vascular system is approximately 10 days. Platelets are supported by multiple regulators including nitrogen monoxide and prostacyclin.[1] Healthy endothelium is essential in contributing to this passive state, because it provides a physical barrier between the circulating platelets and extrinsic activators contained within the walls of the vessel. These extrinsic regulators serve to downregulate platelet responsiveness, preventing inappropriate activation in the passive state. After vascular injury occurs, platelets are the primary cellular component involved in the hemostatic response in an effort to reduce hemorrhage.

The hemostatic response is commonly modeled triphasically as platelet initiation, extension, and stabilization. During initiation, circulating platelets adhere to von Willebrand factor at the site of injury, forming a monolayer. This monolayer of platelets is

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subsequently activated by collagen complexes. Additional platelets are recruited and adhere to the monolayer during the extension phase. Throughout this phase, platelet storage granules are released. The granules contain additional von Willebrand factor. G protein–coupled receptors on these recruited platelets are activated by thrombin, thromboxane A2, adenosine diphosphate, and epinephrine. Once activated, a cascade of events occurs, ultimately leading to platelet aggregation via activation of integrin $\alpha_{IIb}\beta_3$. von Willebrand factor, fibrinogen, and fibrin use the integrin $\alpha_{IIb}\beta_3$ found on the surface of platelets to create crosslinking.[1] The final component of the hemostatic response is known as stabilization. Stabilization occurs partially by increasing intracellular platelet signaling, thus preventing preemptive dissolution. These events lead to the creation of a newly formed fibrin crosslinked thrombus at the site of vascular injury. The newly formed thrombus is capable of withstanding the forces generated by arterial blood flow.

PHYSIOLOGIC PATHWAYS OF THROMBOCYTOPENIA

Thrombocytopenia is defined as a decrease in total platelet count of less than 150,000 platelets per microliter of blood. Thrombocytopenia may be further classified as mild (100,000–150,000 platelets per microliter), moderate (50,000–100,000 platelets per microliter), or severe (<50,000 platelets per microliter). Mechanisms underlying thrombocytopenia can be divided into 4 categories. These categories include increased platelet destruction, decreased platelet production, platelet sequestration, and thrombocytopenia secondary to hemodilutional effects.

Platelet destruction may be caused by autoimmune disorders, which lead to an overall decrease in the lifespan of circulating platelets. Autoimmune disorders may simultaneously blunt the regulatory response of bone marrow to increase platelet production in light of increased destruction, resulting in thrombocytopenia. Platelet destruction also occurs when platelets are physically damaged. Platelet destruction occurs primarily by the following 3 methods: the presence of damaged microvasculature with multiple thrombi, inappropriate platelet activation by proinflammatory cytokines and thrombin, or physical contact with artificial surfaces. Patients with thrombotic thrombocytopenic purpura, low-platelet syndrome of pregnancy, and hemolytic uremic syndrome have damage intrinsic to the microvasculature. Patients with disseminated intravascular coagulation, abnormal vascular surfaces secondary to cardiac valve replacement, aneurysms, and vascular malformations may have a propensity for platelet destruction secondary to inappropriate activation as described above. Artificial surfaces involving cardiopulmonary bypass, intra-aortic balloon pumps, or ventricular assist devices are known to cause structural damage also leading to thrombocytopenia.

As described previously, platelets are produced by megakaryocytes contained within the bone marrow. Pathologic processes affecting the maturation or differentiation of these cells can result in decreased production of platelets, with even greater potentially devastating effects on overall hematopoiesis.

Thrombocytopenia secondary to platelet sequestration also occurs in the clinical setting of hypersplenism. Nearly 30% of platelets are stored in a healthy spleen; however, in cases of splenomegaly, this percentage increases. This splenic-mediated pathologic process ultimately leads to platelet destruction. However, in thrombocytopenia secondary to splenomegaly, the total platelet count typically remains greater than 20,000 platelets per microliter, and significant hemostatic disorders are generally absent.[2]

In addition, thrombocytopenia may be secondary to hemodilutional effects in patients receiving large amounts of fluids without transfusion of platelets. The platelet count can decrease by as much as 50% due to hemodilution when 10 to 12 units of packed red blood cells are rapidly transfused.[2]

Although rare, in consideration of the oral maxillofacial surgeon is the phenomenon of pseudothrombocytopenia, also known as spurious thrombocytopenia. Pseudothrombocytopenia represents an event in which platelet clumping occurs ex vivo, typically in a laboratory setting. It is common practice to add a calcium chelator such as EDTA to a blood sample for anticoagulation effects during laboratory processing. The calcium chelator modifies the response of circulating antiplatelet antibodies targeting platelet surface glycoproteins, resulting in clumping. Automated blood counters fail to recognize these aggregates as platelets, leading to an erroneously low platelet count. Occasionally, the aggregates are further misidentified based on size as neutrophils, resulting in a pseudoleukocytosis. However, this abnormal platelet clumping is recognized in a review of the peripheral blood smear. If clumping is present, a second blood sample may be obtained using alternative anticoagulants such as a citrate or heparin; this usually produces a more accurate platelet count. It is estimated that pseudothrombocytopenia occurs within less than 0.3% of the population without