

# Case 5: Patient Blood Management in a Hematology/Oncology Patient

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## Objectives:

1. Discuss the incidence of anemia in patients receiving chemotherapy.
2. Describe the risks of allogeneic transfusions, including alloimmunization related to transfusion in the hematology/oncology patient.
3. Review the use of adjuncts and alternatives to Red Blood Cell (RBC) and Platelet transfusions in patients receiving chemotherapy.
4. Discuss the role of prophylactic and therapeutic Platelet transfusion in this patient population.

## Case Scenario

*The patient is a 55-year-old male with a 10-month history of squamous cell carcinoma of the larynx previously treated with chemotherapy and radiation. (The last dose of carboplatin was 26 days ago.) He was discharged from the hospital 4 days ago after diagnostic bronchoscopy for newly noted pulmonary nodules suspicious for metastases. Bronchoscopy was equivocal, showing dysplasia but not definitive for malignancy. He is being admitted today after presenting to the emergency room with a 2-day history of chest pain, shortness of breath, productive cough (yellow/green sputum occasionally blood tinged), low-grade fever (maximum temperature 38 C), and fatigue. Laboratory studies on admission are as follows: hemoglobin, 6.7 g/dL; hematocrit, 21.2%; white blood count, 18,400/ $\mu$ L with 92% segmented neutrophils; platelet count,*

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Among the many reasons to limit platelet transfusions are avoidance of infection and alloimmunization leading to the platelet refractory state. A liberal prophylactic Platelet transfusion policy can lead to production of alloantibodies to antigens on the platelet surface (typically HLA Class I) in approximately one-third of patients. This can create a challenge with future Platelet transfusion needs. A poor response to Platelet transfusions as a result of these alloantibodies will require the need for specialized products such as HLA-compatible Platelet units to prevent or control bleeding. The patient described in the clinical scenario was stable and the clinical team decided to hold on giving a Platelet transfusion and employ the use of EACA and vitamin K.

### **What Treatment Is Recommended if the Patient Were to Develop Worsening Hemoptysis and Potential for Pulmonary Hemorrhage?**

The patient's Platelet count is now 12,000 / $\mu$ L. In the Trial of Prophylactic Platelets (TOPPS) the effectiveness of a no-prophylaxis Platelet transfusion strategy against a prophylactic Platelet transfusion strategy among patients with a hematologic malignancy was compared. This randomized, open-labeled, noninferiority study assigned 600 patients to receive Platelet transfusions for platelet counts under 10,000/ $\mu$ L or active bleeding.<sup>28</sup> The incidence of major bleeding was higher in the no-prophylaxis group compared to the pro-

phylaxis group (50% vs 43%), supporting the use of prophylactic Platelet transfusion to reduce bleeding in patients with hematologic malignancy. A subset analysis of patients undergoing autologous stem cell transplantation showed similar rates of bleeding in both groups.

As the patient's hemoptysis worsens and platelet count trends down to 12,000/ $\mu$ L, it is tempting to transfuse Platelet units. Factors to consider when deciding on a therapeutic Platelet transfusion include the level of the platelet count and how rapidly it falls, the acuteness and severity of the bleeding, location of the bleeding source, and the patient's desires. If a decision is made to transfuse Platelets, best practice should be to give 1 dose at a time and then reassess for response and slowing or cessation of bleeding.

One needs to keep in mind that Platelet transfusions have risks, such as sepsis, TRALI, TACO, alloimmunization, and allergic and anaphylactic transfusion reactions. There should be renewed efforts to not only identify the source of bleeding and involve subspecialists who can help in embolization, if needed, but also consider alternative hemostasis options. These alternatives may include DDAVP (1-deamino-8-D-arginine-vasopressin), Cryoprecipitate and recombinant human coagulation Factor VIIa (rFVIIa).

## Therapies of Consideration

### *DDAVP*

DDAVP stimulates the release of von Willebrand factor (VWF) from the endothelium; the released VWF is thought to facilitate clot formation by enhancing platelet adhesion to the vascular subendothelium, particularly in the areas of high-shear stress. DDAVP is a first-line hemostatic agent for mild hemophilia A and von Willebrand disease and has also been used to help control bleeding in patients with acquired platelet dysfunction related to uremia or drugs (eg, aspirin or clopidogrel). Its effectiveness, though, in oncology patients with chemotherapy-induced thrombocytopenia has been less studied.<sup>29</sup>

### *AHF*

Cryoprecipitated antihemophilic factor (AHF) contains Factor VIII, VWF, fibrinogen, Factor XIII, and fibronectin. It is prepared from a unit of Fresh Frozen Plasma and primarily indicated for the treatment of bleeding or the prevention of bleeding before an invasive procedure in patients with hypofibrinogenemia (fibrinogen level <100-125 mg/dL). Treatment of low fibrinogen with Cryoprecipitate commonly occurs for patients with disseminated intravascular coagulopathy (DIC), liver failure, or massive hemorrhage related to trauma or obstetric complications. Ensuring optimal fibrinogen concentration is important for anchoring platelets at the site of injury and clot formation.

### *Factor VIIa*

Recombinant human coagulation Factor VIIa promotes hemostasis by combining with exposed tissue factor and catalyzing a series of reactions on the platelet surface to result in generation of a thrombin burst. It is indicated for the treatment of hemophilia with inhibitors and congenital Factor VII deficiency. It has been used off-label in cases of life-threatening hemorrhage refractory to standard management; however, it should be used with caution due to its thrombotic risk.<sup>30</sup>

### *Thrombopoietic Growth Factors*

In patients with chemotherapy-induced thrombocytopenia, another therapy to consider is the use of thrombopoietic growth factors. For example, oprelvekin (Neumega, Genetics Institute, Cambridge, MA) is a recombinant human interleukin-11 (IL-11) cytokine that stimulates the production of platelets by enhancing the size and ploidy of megakaryocytes. It may be used following chemotherapy in patients who have a high thrombocytopenic risk. It can promote platelet production so as to reduce or eliminate the need for Platelet transfusions and shorten the duration of severe thrombocytopenia.<sup>31</sup> Other novel thrombopoietin-receptor agonists, such as eltrombopag and romiplostim, are being assessed to optimize their dose and schedule in ameliorating chemotherapy-induced thrombocytopenia.<sup>32</sup>

### Key Learning Points:

1. The approach to anemia and thrombocytopenia should focus on simultaneous interventions—stimulate erythropoiesis, enhance hemostasis, and control or prevent ongoing blood losses.
2. Anemia in cancer patients may be multifactorial and treatments should be directed based on etiology.
3. Alternatives to transfusion are available and should be employed, with regard to the special circumstances of oncology patients.
4. Platelet transfusions may be required in the care of patients with cancer, but their use should be restrictive and individualized to limit exposure and risk of alloimmunization.

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