CASE 10.3
Anticoagulation | Level 3

Brady S. Moffett

1. What is the subjective and objective evidence for the diagnosis of arterial thrombosis in this patient?

SUBJECTIVE FINDINGS: Appearance of decreased perfusion (grey, sluggish capillary refill, cold) and distal pulses in that hand were weak.

OBJECTIVE FINDINGS: Doppler ultrasound indicative of decreased perfusion, increased capillary refill time in fingers, weak distal pulses, and cool temperature of fingers.

Risk factors for development of an arterial thrombus include sepsis, underlying coagulopathy, and the presence of arterial catheter.

2. Devise a pharmacologic regimen for the treatment and prophylaxis of arterial thrombosis in a critically ill patient.

The goal for anticoagulation therapy in this patient is to restore perfusion to the affected limb without any major bleeding complications. The patient will have achieved this if the color, temperature, and pulses to the limb have been restored without any serious adverse reactions related to anticoagulation therapy.

Prior to initiation of anticoagulation therapy, any agent responsible for the generation of the arterial thrombus—in this case, the arterial catheter—should be removed if possible. Placement of monitoring catheters in other sites may be an option if they are still deemed necessary.

Unfractionated heparin (UFH) is a suitable first choice of pharmacotherapy because this patient is experiencing signs of decreased perfusion to the limb. UFH can be titrated every 6 hours to attain a therapeutic activated partial thromboplastin time (aPTT) and/or factor Xa concentration. The factor Xa may be a more sensitive test to determine the efficacy of UFH therapy because it is not as easily influenced by disease states. Low molecular weight heparin (LMWH) such as enoxaparin can be used, but because these agents are dosed every 12 hours, the time for titration to a therapeutic concentration may be lengthy. Case series of the use of enoxaparin in arterial thrombus with success have been published.

Tissue plasminogen activator (tPA) can be used to lyse the thrombus if the patient were at immediate risk of losing the limb from the thrombosis. The risk of bleeding is high with use of tPA and should be balanced with the benefit of using tPA. Those at risk of bleeding

include premature infants, patients who have recently undergone a surgical procedure, and patients with baseline bleeding disorders. UFH therapy should be continued during tPA infusion to prevent extension of the thrombus. The risk of bleeding in this patient is high because they are coagulopathic, at baseline, and have reduced drug clearance due to decreased kidney function. The use of tPA should only occur if UFH therapy does not improve perfusion to affected limb within the first 12 hours of therapy or if the perfusion status of the limb decreases significantly while receiving UFH therapy.

For the patient in this case, the use of UFH should occur as soon as possible. Recommended doses of IV UFH should be initiated at 20 units/kg/hr as a continuous infusion, preceded by an IV bolus dose of 75 units/kg (maximum of 5,000 units). Therapy with tPA, should it be required, typically can be initiated at 0.1 mg/kg/hr as a continuous infusion, increasing each hour to a maximum of 0.6 mg/kg/hr over a 6-hour period. The tPA infusion can be discontinued prior to the 6-hour infusion period if perfusion to the affected limb has markedly improved.

3. Determine the appropriate monitoring for the use of anticoagulation therapy in a critically ill patient with an arterial thrombosis.

Standard laboratory monitoring for a patient receiving UFH is the aPTT. A factor Xa assay can be useful in patients with underlying coagulopathy because baseline coagulopathy can affect the aPTT, making the results unreliable in assessing UFH effect. An institution's therapeutic aPTT range is based on a factor Xa concentration of 0.3 to 0.7 units/mL. The factor Xa assay is not readily available at every institution and is typically a resource intensive test, which is not as rapidly available as an aPTT. In this patient, the use of a factor Xa assay would be useful because the patient's underlying disease process (i.e., sepsis) and disease-related coagulopathy would likely alter the aPTT. Initial monitoring would include an aPTT every 6 hours, starting with a baseline aPTT prior to initiation of UFH therapy. Most institutions have a goal aPTT in the 60- to 90-second range for a therapeutic UFH goal, but institutions will vary and the laboratory should be consulted for the specific range. If a factor Xa assay is available and the aPTT appears to be an unreliable measure of UFH effect, factor Xa monitoring should occur at least every 12 hours, with proportional adjustment in UFH therapy to achieve a goal of 0.3 to 0.7 units/mL.

To help determine the validity of an aPTT value in a patient with a disease state that can result in coagulopathy, the use of a heparinase enzyme with the aPTT (HepZyme aPTT) will neutralize the effects of UFH and allow the clinician to investigate the patient's baseline aPTT to assess for coagulopathy. If coagulopathy is present, the HepZyme aPTT will be altered and the results of the aPTT will likely not represent true anticoagulation effect of UFH. In a patient with an altered baseline aPTT, as identified by using the HepZyme aPTT, the factor Xa assay should be used. In situations where advanced coagulation testing (factor Xa assay, HepZyme aPTT) is unavailable, the clinician should be aware of the influences of patient disease processes on laboratory monitoring parameters for UFH.

Monitoring should be continued to assess for bleeding complications, such as a drop in platelets, hemoglobin, or hematocrit, as well as more obvious signs of bleeding, such as oozing from IV cannula sites or bleeding from mucous membranes. Laboratory monitoring for anticoagulation should occur frequently, every 4 to 6 hours in this particular patient, due to their high risk of bleeding. Bleeding from IV cannula sites and mucous membranes can be assessed on a continual basis in the intensive care unit. Similarly, neurologic status should be monitored continuously to assess for intracranial or intracerebral bleeding. Sudden or dramatic changes in neurologic status, such as a seizure or change in neurologic exam, would warrant the use of advance imaging techniques for occult bleeding.

Platelet monitoring during UFH therapy is necessary to detect heparin-induced thrombocytopenia (HIT), a rare but devastating complication in pediatric patients receiving UFH. HIT Type I is characterized by a slow decrease in platelets and is due to platelet consumption or