Transfusion Associated Circulatory Overload

Plasma is most often transfused to reverse a coagulopathy in a patient who is bleeding or scheduled to undergo an invasive procedure. It is also used as a replacement fluid during plasma exchange for treatment of diseases such as TTP or myasthenia gravis. In 2011, Saint Luke’s Health System hospitals transfused more than 4500 units of plasma. The May 2012 issue of the Clinical Laboratory Letter summarized the evidence that it is not usually necessary to correct a mildly elevated INR of 1.7 or less prior to an invasive procedure. In spite of this evidence the transfusion service continues to receive orders for plasma transfusion in nonbleeding patients with mildly elevated INRs.

Unfortunately, some of these plasma transfusions have been associated with adverse reactions. The most common risks associated with plasma transfusion include allergic reactions, transfusion related acute lung injury (TRALI) and transfusion associated circulatory overload (TACO). The incidence of TRALI has declined significantly in the past 2 years following the introduction of male-only plasma, but the incidence of TACO appears to be increasing both locally and nationally.

Active surveillance of plasma recipients indicates that TACO is a relatively common, but often unreported, occurrence. Between 4 and 5% of plasma recipients experience symptoms consistent with TACO. The estimated risk is 1 reaction per 70 units of plasma transfused. TACO reactions can be life threatening. Published mortality rates range from 5 to 15%. The latest Food and Drug Administration transfusion related mortality report indicated that TACO accounted for 20% of reported deaths.

TACO usually occurs when plasma is infused too quickly or in high volume. Generally, it is recommended that plasma be infused at a rate of 250 to 500 mL per hour. This is equivalent to one bag in 30 to 60 minutes. More than 50% of patients who develop TACO were transfused at a higher rate. TACO cases occur most commonly in ICU patients. These patients may be predisposed to volume overload due to their comorbidities including congestive heart failure, renal failure, respiratory failure and positive fluid balance.

Signs and symptoms include dyspnea, orthopnea, wheezing, tightness in the chest, cough, cyanosis, tachypnea, rapid increase in blood pressure, distended neck veins, and S3 on auscultation. Peripheral and pulmonary edema may also develop. Chest x-ray demonstrates bilateral infiltrates and possibly an enlarged heart. BNP is usually elevated. If a pre and post BNP level are available, the post BNP level usually increased by at least 50%.

At the first indication of TACO, the patient should be placed in a sitting position and the transfusion stopped. If symptoms progress oxygen support and IV administration of a rapid acting diuretic may be necessary. Unlike TRALI, most patients with TACO will rapidly improve with diuresis. If symptoms are severe and urgent, a therapeutic phlebotomy of 200 to 400 mL may be warranted.

TACO can be prevented by limiting the total volume of crystalloid and colloid infused as well as the rate of infusion. Patients with risk factors for circulatory overload should probably have their plasma infusion rate reduced to 1 mL per kg body weight per hour. Diuretics can also be given prior to transfusion.

Pneumococcus Antigen for CSF

Urine antigen testing is a useful adjunct in the diagnosis of pneumococcal pneumonia, with sensitivity and specificity approximately 86% and 94%, respectively. *Streptococcus pneumoniae* antigen testing on CSF specimens from patients with suspected pneumococcal meningitis is now available through Saint Luke’s Microbiology as well. Sensitivity and specificity of pneumococcal CSF antigen testing is approximately 97% and 99%, respectively, compared to culture. The performance characteristics of this assay are unknown in patients who have been treated with antibiotics for more than 24 hours prior to specimen collection.

Misleading Test Results Post-Transfusion
Recently, the clinical pathologists have been asked to investigate two different cases where laboratory results did not support clinical findings. In the first case, a patient was admitted with a hemoglobin of 6.5 g/dL. CBC revealed low MCV and MCHC consistent with a hypochromic microcytic anemia. The patient was symptomatic and transfused with 2 units of red blood cells. The next morning, blood was drawn for iron studies. Both serum iron and transferring saturation were within normal limits. A unit of red blood cells contains 200 to 250 mg of iron. At least 25% of this iron is released from senescent donor cells during transfusion. It is important to realize that iron studies can be normalized in iron deficient patients following transfusion. Iron studies should always be ordered and collected prior to transfusion.

Many other chemistry tests can be affected by recent transfusion. The release of hemoglobin from transfused red cells can also increase total and unconjugated bilirubin and decrease haptoglobin for up to 24 hours. Transfused red blood cells also contain high concentrations of lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and potassium that may be released from older red cells during transfusion. Enzymes can remain elevated up to 24 hours post-transfusion. Potassium can be transiently increased during massive transfusion. Ionized calcium may be transiently decreased due to the citrate, which is used as an anticoagulant in donor blood.

Another interesting case involved a patient who was admitted with diffuse alveolar hemorrhage. Plasma exchange was immediately started upon admission. In spite of this clinical presentation, all autoantibody studies were normal. Further investigation revealed that all of the specimens for autoantibody testing had been drawn the next morning after the first plasma exchange. Repeat testing on a specimen obtained prior to plasma exchange revealed significantly elevated ANA titer and anti-DNA antibody.

During plasma exchange, a patient’s plasma is removed and replaced with donor plasma. Typically, 10 to 12 units of plasma are transfused per episode. Each procedure removes between 65 and 80% of all plasma constituents. Plasma exchange is usually repeated daily or every other day. Most plasma protein levels, such as complement or enzymes, remain low for at least 3 days. It is especially important to realize that immunoglobulin levels do not return to pre-exchange levels up to 2 weeks post-exchange. Thus, one must be especially careful interpreting infectious disease serology and autoimmune studies in patients undergoing plasma exchange.

**Influenza—Abundant & Early**

The Centers for Disease Control reports increasing influenza activity since early December in all regions of the U.S. except the southwest. Influenza A is predominant in the northeast, north central and Pacific northwest states. Influenza B is predominant in the Rocky Mountain region as well as the south central U.S., while the southeastern states have a mixture of influenza A & B. The region including Missouri, Kansas, Iowa, and Nebraska reports a mixture of A & B as well, however Missouri has influenza B predominantly. According to the CDC, the 2012-2013 Northern Hemisphere influenza vaccine is well-matched to the currently circulating influenza strains. Likewise, no resistance to oseltamivir or zanamivir has been detected to date.

Saint Luke’s metro hospital laboratories have reported 107 positive rapid influenza antigen tests since December 1, with 86 tests positive for influenza B and 21 tests positive for influenza A. This is reflective of influenza activity detailed by the Missouri state public health laboratory, which for the week ending December 15, reported 991 cases of influenza B and 109 cases of influenza A. CDC has typed the influenza B strain as B/Wisconsin/01/2010-like.