

## **PULMONARY EDEMA AFTER RAPID TRANSFUSION OF FFP: ANSWERS**

**A case history by Jim Perkins, M.D. (© 2009)**

### **Question:**

1. Is FFP indicated for this patient? Is there anything else you might want to do for the patient?

*The patient has a severe coagulopathy due to her warfarin therapy, and is at risk for bleeding spontaneously. Plasma transfusion is often given to such patients in order to correct the prothrombin time (PT). However, the duration of action of plasma is relatively short, about 4 hours. The patient has had this degree of coagulopathy for weeks, so in order for plasma transfusion to be rational at this particular time, there would have to be something special about the next 4 hours such as an operation to be performed within that time period. Unless the patient is bleeding or is about to undergo an invasive procedure plasma is not generally considered to be indicated according to the transfusion guidelines of multiple organizations.*

*Vitamin K administration will reverse the coagulopathy caused by warfarin, and because of the relatively short half life of factor VII, the PT will begin to correct within 10 hours. However, since the patient is not bleeding and has a clear indication for anticoagulation, complete correction of the PT is not desired. Instead, the appropriate goal would be to bring her back to a therapeutic anticoagulation level. In the long term, patient's warfarin dosage needs to be adjusted. This is, of course, challenging given the multiple drugs such patients take and the capacity of many agents to alter warfarin metabolism.*

*One course would be to simply stop the warfarin and allow the PT to correct on its own. In well nourished patients this may take 3 to 4 days, but can take much longer if the patient does not have an adequate vitamin K intake. In a patient with a PT/INR this high or with poor vitamin K intake, low dose vitamin K should be given in an attempt to bring the PT down relatively quickly, but not to completely reverse the warfarin anticoagulation. Low dose vitamin K in this context consists of 1.25 to 2.5 mg given orally. The INR should then be followed. Once the level is back into the therapeutic range, warfarin can be resumed at a lower dose.*

2. What is the differential diagnosis of this transfusion reaction? Are there any laboratory values which could help make a diagnosis?

*The patient developed respiratory failure due to pulmonary edema after transfusion of 720 mL of FFP over one hour and 25 minutes. Although some degree of respiratory embarrassment may be seen with a number of different types of transfusion reaction, severe respiratory failure due to pulmonary edema is characteristic of two types, transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO).*

*B-type natriuretic peptide (BNP) is an analyte that is secreted by ventricular myocytes in response to stretch. It is often increased in patients with congestive heart failure. Detection of an increase in the level of BNP between pre- and post-transfusion blood specimens may be seen in TACO. However, assays for BNP were not generally available at the time of this case.*

*Although there may be multiple mechanisms of TRALI, the one that is best documented begins with donor antibody directed against recipient leukocyte antibodies which leads by some process to activation of neutrophils producing a capillary leak syndrome and non-cardiogenic pulmonary edema. Anti-leukocyte antibody specificities that have been implicated in TRALI include those directed against class I and class II HLA and certain neutrophil-specific antigens. Typically these antibodies are found in gravid women and are thought to have been made in response to exposure to the corresponding antigens expressed by fetal leukocytes, but blood donors who have previously received a blood transfusion have been implicated as well. Therefore when recipients develop a clinical syndrome consistent with TRALI investigation often begins with an inquiry into the demographics of the donor, specifically whether the donor is a woman with one or more pregnancies or whether the donor was ever transfused. If the donor is in one of the risk categories, the next step would be to screen donor plasma for anti-leukocyte antibodies. If multiple components were given within the 6 hours preceding the patient's first symptoms, multiple donors may need to be tested.*

**3. In view of this new data would you change your answer to either of the previous questions? What is your diagnostic impression?**

*The clinical history and autopsy findings are consistent with TACO with a classic description of frothy edema at the time she went into respiratory failure and on autopsy. The long history of poorly compensated CHF corroborated by the ischemic cardiomyopathy diagnosed at autopsy constitutes a typical clinical substrate for this reaction.*

*TRALI was not mentioned as a possibility by the clinicians at the time of the patient's reaction or by the autopsy pathologist, so even if it was considered, no testing was done to investigate the possibility. Nonetheless, there is no evidence to corroborate TRALI as a cause of the pulmonary edema. Specifically, the patient did not develop fever. The WBC count is not low on the CBC drawn immediately after the reaction (there is no pre-transfusion WBC count in the record). Finally, the autopsy pathologist stated that there was no microscopic evidence of pneumonia, presumably meaning that he did not see neutrophils in the lung parenchyma, a pathologic feature of TRALI.*

*For these reasons this case is presented as a fatal case of TACO. Many studies demonstrate the dangers of transfusion in critically ill patients, and pulmonary complications are a major component of the problem. TACO is one of the most preventable of transfusion reactions. RBCs are often transfused in pairs when there is little urgency. When patients have conditions predisposing them to circulatory overload such transfusions can be separated by several hours in order to allow time for the patient to equilibrate, with or without the help of diuretics. In fact, if the time between transfusions is utilized for performing a blood count, in many cases the second unit may prove unnecessary (c.f. A Transfusion Related Respiratory Event). As discussed above, there was no urgency in this case, and the order to transfuse two units of FFP "as rapidly as possible" was inappropriate.*