

A FEBRILE REACTION IN A WOMAN WITH ANTI-Fy^b; ANSWERS

Case study by Jim Perkins (©2009)

1. What is the differential diagnosis of fever at the time of transfusion?

Fever during or soon after transfusion may either be due to the transfusion or may be coincidental to transfusion and due to the patient's underlying disease. Fever due to transfusion is most commonly a febrile non-hemolytic transfusion reaction (FNHTR) which may have different pathogenic mechanisms. FNHTRs in patients with antibodies against donor leukocytes have long been recognized. Indeed, antibodies against HLAs were first demonstrated in thalassemic patients who routinely experienced fever when they were transfused, presumably when destruction of donor leukocytes released endogenous pyrogens, now recognized as inflammatory cytokines. More recently it has been demonstrated that release of cytokines into blood components during storage may cause fever. Of note, fever is the most common symptom of a hemolytic transfusion reaction (HTR). Bacterial contamination of the unit also causes high fever, often with hypotension. Fever is a common symptom of transfusion related acute lung injury (TRALI), although the presence of respiratory symptoms overshadows the fever.

2. What steps should be taken to investigate this fever?

Because of the importance of hemolytic transfusion reactions and detection of inadvertent blood group incompatibility, transfusion reaction investigation focuses on ruling them out. This typically begins at the patient's bedside with a clerical check to make sure that the unit was indeed intended for transfusion to the individual receiving it. The offending unit and a post-transfusion recipient blood specimen should be submitted to the laboratory. A negative direct antiglobulin test (DAT) and negative inspection of the post-transfusion plasma for hemoglobin or bilirubin virtually rules out an HTR, but AABB standards requires repeat blood typing from the post-transfusion specimen as well. Some laboratories also routinely culture any residual blood for bacteria.

3. What steps should be taken to care for the patient?

The most important patient care issue is simply to stop the transfusion. Antipyretics may be given, and severe rigors often respond to meperidine. FNHTRs are generally self-limited. Other responses may depend on the findings of the transfusion reaction investigation and clinical judgment. If hemolysis is demonstrated the patient should receive saline and furosemide to support her urine output.

4. What manifestations of a HTR did this patient present? Was diphenhydramine an appropriate treatment for this reaction?

Transfusion reaction evaluation demonstrated that one of the two units of RBCs the patient received was incompatible with the anti-Fy^a demonstrated before transfusion.

As mentioned, fever is the most common manifestation of a HTR.. Chills often accompany fever, and nausea is well-described as a symptom of a HTR. However, confusion is not generally part of such a reaction, although it might be expected in patients who develop shock. Instead, the confusion appeared to relate to diphenhydramine administration. Diphenhydramine is often given to patients prior to transfusion even when they do not have a history of allergic reactions, and to patients having febrile reactions. This practice should be discouraged. Antihistamines should be reserved for prevention or treatment of allergic reactions. Diphenhydramine frequently causes confusion in older patients and may cause idiosyncratic reactions at any age.

The graph of the hemoglobin level demonstrates an increase of 4.9 gm/dL after transfusion, followed by a fall of about half that over 12 hours, consistent with near-complete destruction of one of the two units

transfused. Other evidence of hemolysis included the increase in the unconjugated bilirubin fraction, measured as an increase in the difference between the total bilirubin and the "direct-acting" bilirubin levels. Of note, the elevation in the total bilirubin level peaked and receded quickly as unconjugated bilirubin was metabolized and excreted. The LDH level also increased, but the single haptoglobin level measured after the incompatible transfusion was normal, presumably because the hemolysis was largely extravascular.

Other effects of this HTR can be seen in the patient's hematologic test results. The increase in the WBC count emphasizes the fact that HTRs cause a systemic inflammatory response. The platelet count fell and the prothrombin time (PT) increased slightly, as is often seen, presumably as a manifestation of subclinical disseminated intravascular coagulation (DIC). A major concern was that the HTR might affect the patient's renal function, perhaps causing long-term irreversible damage. Although there was a suggestion of an increase in the patient's creatinine level and urine output were well maintained

The patient was informed of this error.