

Podcast 34: Managing Febrile Transfusion Reactions

Tony Casina:

Welcome to QuidelOrtho Science Bytes. We're proud to sponsor this podcast as a continuing commitment to transform the power of diagnostics into a healthier future for all. Today, our topic is, what is a febrile transfusion reaction and how are they managed? I am Tony Casina, and today, I am joined by Dr. Aaron Tobian. Dr. Tobian is a professor of pathology medicine and epidemiology at the Johns Hopkins University School of Medicine and Bloomberg School of Public Health. He is also director of the Transfusion Medicine Division and vice chair for clinical Affairs in the department of pathology at Johns Hopkins Hospital. Dr. Tobian divides his time between research and clinical service. Over the past 15 years, Dr. Tobian has lived or worked in five developing countries. He has authored more than 300 peer-reviewed journal articles. Thank you so much for joining us today, Dr. Tobian.

Aaron Tobian:

Thank you very much for the invitation, Tony. It's wonderful to speak with you.

Tony Casina:

Okay. Let's get started with the first question. What is a transfusion reaction, and what are the different types of transfusion reactions?

Aaron Tobian:

Thank you, Tony. Transfusion reactions are adverse events that are associated with blood transfusion, and for the average hospitalist, they're incredibly common. We often see transfusion reactions associated with 1% to 2% of all blood transfusions, and they can range from either a mild fever to even a life-threatening hemolysis. So it's incredibly important to understand the etiology and quickly treat the reaction. The goal is to prevent any harm from the reaction, but also to understand what caused the reaction and how can we prevent additional reactions. Specifically, the CDC hemovigilance defines febrile reactions as at least a 1-degree increase in Celsius that's above 38 degrees Celsius. In terms of what is the etiology or the cause of febrile transfusion reactions, there could be many different types of reactions.

One possibility is acute hemolytic transfusion reactions. They're associated with ABO-incompatible blood transfusion. You can have febrile non-hemolytic transfusion actions. You can have transfusion-related sepsis or bacterial contamination of the blood product that leads to a very high spiking fever. You can have TRALI or transfusion-related acute lung injury that can present with respiratory symptoms, or the fever could actually be the underlying disease. Many oncology patients who are receiving platelets have febrile neutropenia and are spiking fevers continuously. So there are many etiologies of a febrile reaction associated with transfusion during that interval.

Tony Casina:

Okay. Thank you, Dr. Tobian. So how do you approach this type of reaction in a patient?

Aaron Tobian:

The critical aspect is number one, you need to assume all reactions are an ABO-incompatible hemolytic transfusion reaction. Number one, two, and three steps, as I always teach my medical students, is to stop the transfusion. You do not want to cause any additional harm. If it is an ABO-incompatible transfusion reaction, you want to limit the amount of blood you're providing. If it's a septic transfusion reaction, you want to limit the number of bacterial contamination products that you're transfusing.

So number one is you absolutely stop the transfusion. However, it's also important to understand the clinical context.

What are the patient's symptoms? Is it just a fever? How high is the fever? Septic reactions usually come on very fast with a very high fever. Is there any hypotension or shock that can be associated with an ABO-incompatible hemolytic transfusion reaction, or is there a possible respiratory failure that can be associated with TRALI? In addition, we want to think about what are the types of blood products? Is it a red cell product that can lead to an ABO-incompatible hemolytic transfusion reaction? Plasma and platelet products are less concerning for acute hemolytic transfusion reactions. Platelet products are also more concerning for septic transfusion reaction. So we want to understand what was actually given to the patient, and then how was the product possibly manipulated? Was it leukocyte-reduced? Was it pathogen-reduced? And these can reduce some of the different types of transfusion reactions.

And the other question we always think about is, what is the clinical context? Was the patient spiking fevers in the last 24 to 48 hours, or was this patient totally stable and fine over the hospital course?

Tony Casina:

Okay. Thanks, Dr. Tobian. What type of workup is performed to evaluate this type of reaction, whether it's specific tests that the transfusion service and laboratory can perform for these evaluations?

Aaron Tobian:

So as I'd mentioned previously, the most critical aspect is to rule out an ABO hemolytic transfusion reaction. And so all the initial testing is really focused on, could this be incompatible blood product? And this is most often caused by either clerical error.

So the first aspect is, is there dramatic hemolysis? And you can do this by looking for hemoglobinemia. If you've got a surgical patient, you often can look in the Foley catheter, and has all the urine turned red? That's the key understanding for someone who is in the operating room. But we can also look at that for blood samples. We also want to do a clerical check. We look through the electronic medical record. We look at the paperwork to check to ensure the correct unit went to the right patient. Often, with ABO-incompatible hemolytic transfusion reactions, you have someone who had one tube of blood that was drawn and it was either mislabeled or improperly labeled, and so you have an incorrect blood type for that person.

One way to figure this out is to also evaluate a post transfusion sample. And in the blood bank, we always repeat the ABO and Rh testing for all of our febrile hemolytic transfusion reactions or non-hemolytic transfusion reactions. We want to make sure that if the patient was blood group O, post transfusion, we're also seeing the patient is blood group O. And one of the initial tests is also the direct antiglobulin test or the DAT or also known as the direct Coombs. And there, we're looking for the coating of red blood cells with antibody to determine whether this is an antibody-mediated reaction. After ruling those out, we often want to look at, could this be possible sepsis? So we usually send the bag and the post transfusion sample to the micro lab to do a bacterial culture. If all these tests are negative and the patient doesn't have respiratory symptoms, the patient likely either has a febrile non-hemolytic transfusion reaction, or the cause of the reaction is actually the patient's underlying disease that's causing the fever.

Tony Casina:

Okay. So what mechanism is involved in these types of febrile reactions?

Aaron Tobian:

I think it's important to focus on the febrile non-hemolytic transfusion reaction. And this is a reaction that's caused by increased cytokines or actually protein in the blood that leads to an increase in the recipient's temperature. And this is most often caused by cytokines TNF-alpha, IL-1-beta, and IL-6 that are produced from the white cells. Cytokines can either be secreted during the storage, so before transfusion, so it's either a pre-formed substance, or alternatively, cytokines can be secreted after the transfusion. This is most often caused by recipient HLA antibodies that can attack the red blood cells or by donor antibodies that attack the recipient white blood cells.

Tony Casina:

What can be done to reduce this type of non-hemolytic reaction that produces reactions of this nature in a patient?

Aaron Tobian:

Well, one aspect is we can use Tylenol pre-medication, and this may mask the fever. However, it does not totally prevent the reaction. With that being said, my theory is, if the patient has not experienced a fever or symptoms, clearly the patient is having a better transfusion experience, and I'm totally supportive. However, the best way to really prevent febrile non-hemolytic transfusion reactions is to use pre-storage leukocyte reduction.

About 15 years ago, Johns Hopkins Hospital conducted a study, and we evaluated the number of allergic transfusion reactions and febrile non-hemolytic transfusion reactions as our institution moved from 100% non-leukocyte-reduced products to 100% pre-storage leukocyte-reduced products. During that time period of over two years, we found that the allergic transfusion reactions stayed the same. So our reporting of reactions throughout the hospital was constant. However, as we moved to 100% leukocyte-reduced products, the number of febrile non-hemolytic transfusion reactions reduced by about 50%. So what we're doing is we're removing those white cells prior to storage, so then there are less white cells that are secreting cytokines during the storage. And that is the best way to prevent a febrile non-hemolytic transfusion reaction.

Tony Casina:

That's a pretty dramatic drop and very favorable for patients. Okay. So to close out this conversation, how can transfusion medicine laboratories help the clinician to manage situations that involve this type of transfusion-related reaction when they occur?

Aaron Tobian:

The transfusion medicine laboratory is used to febrile non-hemolytic transfusion reactions and other adverse events associated with the transfusion. However, many clinicians, this could be their very first experience dealing with adverse events associated with transfusion. So it's very important for the collaborative team and the medical director to engage with the clinical team and to work collaboratively.

It's important to rule out the most critical types of febrile reactions associated with transfusion, the acute hemolytic transfusion reaction, transfusion-related sepsis and TRALI, and then it's important to educate the clinician, how are the best ways to treat these different types of reactions? Or if it's a febrile non-hemolytic transfusion reaction, how do you ensure that you're providing the best blood products in the future to provide the best transfusion experience?

Tony Casina:

Well, thank you, Dr. Tobian. I really want to thank you for taking the time with us today and giving us your experiences and insights on this fascinating topic. It has been a pleasure to talk with you. And again, thank you so much for your time today on this podcast.

Aaron Tobian:

Thank you, Tony. It's been wonderful to talk with you about febrile reactions associated with blood transfusion.

Tony Casina:

Yes, quite the interesting topic. I hope you all enjoyed this broadcast episode about febrile non-hemolytic transfusion reactions and the challenges that they present to the transfusion service. Make sure to review the sections within the

podcast description for any reading materials that we've suggested. Based on today's podcast, I'll leave you with our pop quiz. What might be the best solution to reducing febrile non-hemolytic transfusion reactions? You can always go back and listen again. Thank you for listening, and please subscribe to QuidelOrtho Science Bytes, brought to you by QuidelOrtho Corporation, where we are transforming the power of diagnostics into a healthier future for all. Take care. Stay healthy and safe.