CD Summary

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OCULAR REACTIONS FOLLOWING TRANSFUSION OF LEUKOCYTE-DEPLETED BLOOD

On December 23, 1997, the Portland office of the American Red Cross blood bank notified the Health Division about a cluster of possible transfusion reactions at a hospital in southwest Washington. Unfortunately, all of the initial identified patients were Washington residents, and the investigation was graciously if reluctantly ceded to our colleagues to the North. The FDA (which regulates the blood supply industry) was notified. The initial investigation confirmed that something was indeed going on, and soon led to the identification of other possible cases elsewhere, including Oregon. The following report contains preliminary findings from this ongoing investigation, now a national one with major roles by the Washington Department of Health, the CDC, the Red Cross, the FDA, and, of course, your Health Division. We begin with two representative case reports.

Case 1. A 78-year-old man with a history of repeated blood transfusions (for his myelodysplasia-induced anemia) received 2 units of leukocyte-depleted red blood cells. No problems were noted during his afternoon transfusion and the rest of his day was uneventful. The next morning he awoke with impressively "bloodshot" eyes, eye pain, and photophobia; signs and symptoms severe enough to warrant a same-day evaluation by his primary physician. He was referred to an ophthalmologist, diagnosed with moderate to severe bilateral iritis, and sent home with steriod eye drops. His symptoms slowly resolved over the next 10 days. The patient returned for a scheduled transfusion three weeks later, and again suffered a similar reaction.

Case 2. A 39-year-old woman received 2 units of leukocyte-filtered red blood cells because of a malignancy-related anemia. Within 24 hours, she developed bilateral red eyes and minor eye pain. She attributed both to "environmental allergies." Her symptoms were mild and resolved in 5 days without medical attention.

OUTBREAK OVERVIEW

Although scattered reports have been received from other parts of the country, the bulk of the reported cases and, coincidentally, the most intensive investigations, have occurred in Oregon, Michigan, and Washington. As of January 7, 1998, 49 transfusion-related red-eye reactions (aka "ojos rojos syndrome") have been identified in those three states, occurring in 38 patients. The Oregon patients are scattered throughout the state, with a small cluster in the Salem area. For investigational purposes, we defined a case of ojos rojos syndrome as the occurrence of bilateral eye redness on or after November 1, 1997 and within 24 hours of receiving a red blood cell transfusion product (RBC).

These patients are not being transfused because of surgery or trauma; all have some kind of underlying hematologic or oncologic disease for which repeated transfusions with leukocyte-depleted red blood cells may be required. The median age of cases in the three investigation states was 59 years (range, 28-84); 22 (58%) were male. The median time from transfusion initiation to symptom onset was 20 hours (range, 1-24 hours). Reactions were characterized by conjunctival erythema or hemorrhage (100%), eye pain (62%), headache (25%), eye edema (23%), arthralgia (19%), and nausea (15%). The median duration of symptoms was 5 days (range, 2-21 days). No deaths or permanent eye sequelae have been identified to date. Specific transfusion information was available for 45 reactions; in each instance the patient had received at least one unit that had been leukocyte reduced with the LeukoNet™ Prestorage Leukoreduction Filtration System (HemaSure, Inc; Marlborough, Mass.).*

Leukocyte-reduced red blood cells are an increasingly common transfusion product. Since leukocytes are the predominant antigen reservoir in RBC transfusions, leukocyte filtration is thought to reduce the chance of alloimmunization in patients who require repeated transfusions. Leukocyte filtration is done either prior to distribution of blood products to local blood banks (prestorage filtration) or at the recipient's bedside. Prestorage filtration removes over 99% of the leukocytes.[1] The majority of Oregon patients who receive leukocyte-reduced blood products are given prestorage filtration RBC units.

The pathogenesis of the ojos rojos syndrome is unknown at this time. The time course, symptomatology, and—in many cases—resolution without treatment makes an infectious cause or crossmatch problem unlikely. The best guess today is an allergic or toxic response to a substance present in the RBC transfusion. The identification of this mystery substance and its source are the questions of the day.

From November 1, 1997 through January 15, 1998, the Portland blood bank distributed approximately 5,000 leukocyt-depleted red blood cell units; ~80% were filtered with LeukoNet devices. These products were distributed throughout Oregon and southern Washington. Why then, have there been only two dozen, somewhat geographically clustered reaction reports? The answer is uncertain, but there are several issues to consider. First, the mild nature of patients' symptoms and the offhanded nature of reaction "reporting" leads us to suspect that many patients may have had reactions that they attributed to allergic or infectious conjunctivitis and subsequently failed to report to their physicians. Second, this syndrome is not a previously recognized type of transfusion reaction and therefore may not have met local criteria for reporting transfusion reactions, and clinicians may not have recognized an isolated red-eye presentation as being related to a recent transfusion. Again, these are patients with complicated medical histories. Several cases have been discovered only through active surveillance with Oregon oncologists or when patients called in after hearing about the problem in the media.

* use of a trade name does not imply endorsement by the OHD (duh).

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To date, there is no evidence that specific practices at any particular hospital or clinic are associated with the risk of reaction. No patient characteristics (e.g., underlying medical condition, concurrent medications, allergies) have been identified that are associated with risk. The answer may lie in the production and distribution of the filters and the filtered products. To date these reactions have only been associated with LeukoNet filters. Our investigation is currently focused on identifying suspect filter lots and filter components, and the subsequent distribution of blood products processed with these devices.

WHAT'S THE POINT?

Why such enthusiasm for a relatively mild and self-limited reaction? While many patients described mild symptoms of little consequence, others reported more severe problems with visual disturbance and severe pain lasting as long as two weeks. Such reactions can be debilitating for anyone, much less older persons with underlying hematologic or oncologic illness. Moreover, this outbreak serves as a reminder of the need for constant vigilance regarding the nation's blood supply. Blood products are widely used. The Portland ARC facility distributed over 46,000 red blood cell units between November 1, 1997, and January 15, 1998. There is already enough concern about the risk of bloodborne pathogens from transfusion products. Public health agencies must be aggressive in safeguarding the integrity of blood products.

On New Year's Eve, 8 days after the initial reports, the Red Cross issued a nationwide voluntary embargo of filtered blood products associated with seven lots of LeukoNet prestorage filter devices. On January 7, 1998, the embargo was expanded to include all LeukoNet-filtered blood products processed since October 1, 1997. To our knowledge, no new cases of ojos rojos syndrome have occurred since that date. The investigation continues. Our readers are reminded that if you have seen or heard of similar cases in your practice and haven't yet told us (or your local blood bank) about them, don't hold back. Operators are standing by to take your calls (503/731-4024).

REFERENCE

Some of the material in this article was derived from a recent MMWR article: CDC. Adverse ocular reactions following transfusions—United States, 1997-1998. MMWR 1998;47:49-50.

1. Lane TA, Anderson KC, Goodnough LT, et al. Leukocyte reduction in blood component therapy. Ann Intern Med 1992;117:151-162.

Influenza Update

THIS SEASON BEGAN with all the excitement and pandemonium of the 1976 swine flu outbreak. Viral genetic engineers concocted their worst in the form of "chicken flu"—influenza A(H5N1)—releasing the bomb in Hong Kong. Circumstances were ideal for another viral conquest. Unfortunately (from the viral perspective), H5N1 seems to lack the ability to be readily transmitted from person-to-person, and to date has not been reported among humans outside Hong Kong. Given the cunning habits of these viruses, this could still occur at some point with the emergence of a true pandemic threat. A total of 18 confirmed H5N1 cases (six fatal) have been reported. The last known case had onset on December 28, 1997.

Amidst this diversionary feint, influenza A/Sydney was quietly invading the U.S. using the age-old method of ship spread—perfected in the plague years. A/Sydney was prevalent in Australia and New Zealand during the past season, and an outbreak caused by A/Sydney was reported among the passengers and crew of a cruse ship that docked in New York City last September. (Coincidentally, the first isolate of A/Sydney/05/97-like [H3N2] in the continental US was obtained from a New York infant.) A/Sydney is related to but distinguishable from A/Nanchang/933/95 , which is the A(H3N2) component of the 1997-1998 influenza vaccine. The protective efficacy of this year's vaccine against A/Sydney is unknown, but is presumably less than ideal. Nonetheless, it is too late to do anything about it this year, as decisions about vaccine composition must be made almost 9 months before the season begins. Subsubtyping of viral isolates is not widely available and few U.S. isolates have been characterized to date. Of the 72 influenza A(H3N2) viruses collected since September 28 that have been studied by CDC, 28 (39%) are similar to A/Wuhan; the remaining 44 (61%) are similar to A/Sydney. The proportion of A/Sydney-like viruses has increased each month. Of 648 type A isolates subtyped nationally, only one has been A(H1N1). Eight type B isolates have also been found.

Here in our own pasture, herd immunity has undoubtedly blunted transmission. By the end of January, the OSPHL reported 31 recoveries of type A virus from 252 specimens of epidemic catarrh. Although the proportion due to A/Sydney will probably not be known for some time, only one of the 20 cases for whom immunization data were available had been vaccinated, suggesting that if A/Sydney is present, it is not yet overwhelming our defenses.