Fatal transfusion-transmitted infection due to *Citrobacter koseri*

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BACKGROUND: Transfusion-transmitted bacterial infection (TTBI) is still one of the most feared complications of blood transfusion.

CASE REPORT: We report a fatal case involving an 8-year-old child with congenital dyskeratosis complicated by severe aplastic anemia who was regularly transfused with platelet (PLT) concentrates for 5 years. The patient received an apheresis PLT concentrate (APC) on Day 0 due to thrombocytopenia complicated by mucocutaneous hemorrhage. Thirty minutes after the start of the transfusion, bradycardia and dyspnea appeared, quickly followed by chills, nausea, vomiting, headache, and hyperthermia. TTBI was suspected and the patient was immediately treated with intravascular antibiotherapy. On Day 3, the patient developed severe acute respiratory distress syndrome leading to death on Day 7. Patient blood cultures and APC cultures were both positive for *Citrobacter koseri*.

RESULTS: The donor was a 19-year-old woman. She had previously given blood. No infectious symptom was reported during the medical interviews before and after the donation and no postdonation information was received. On the day of the donation (Day −2), her white blood cell count was 5.83×10^9/L. She came back on Day 8 to undergo additional tests. The cultures from blood, stool, urine, the skin of the inside of the elbow at the point of needle insertion, and ear samples were all negative for *C. koseri*. However, a nasal sample was positive for *C. koseri*.

CONCLUSION: The isolates from the donor's blood cultures, the APC bag, the attached tube, and the donor's nasal sample all gave identical profiles; they were thus identified as the same strain and the TTBI was confirmed.

Bacterial transmission by blood transfusion is a rare adverse event (0.19/100,000 blood products transfused, ANSM, French National Agency for Medicines and Health Products Safety, 2013), but is feared due to its potential severity. Bacterial detection or inactivation of blood components could substantially reduce or even eliminate the complication. However, such measures are not currently mandatory in France and only performed in some blood centers. We report a fatal case transmitted by an apheresis platelet concentrate (APC). Investigations found the bacterium responsible at an unusual location in an otherwise healthy donor.

CASE REPORT

An 8-year-old child suffering from congenital dyskeratosis[1] complicated by severe aplastic anemia was regularly transfused with PLT concentrates for 5 years. On February 18, 2015 (Day 0), she was given an APC, due to thrombocytopenia of less than 10×10^9/L responsible for mucocutaneous hemorrhage of Grade 2 according to World Health Organization staging. The white blood cell (WBC)

ABBREVIATIONS: APC(s) = apheresis platelet concentrate(s); rep-PCR = repetitive sequence-based polymerase chain reaction; TTBI = transfusion-transmitted bacterial infection.

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count was 0.25×10^9/L. No fever was observed before transfusion but the patient was given prophylactic antibiotics (itraconazole and sulfamethoxazole/trimethoprim). Thirty minutes after the start of the transfusion, the patient experienced bradycardia (54 bpm) and dyspnea (oxygen saturation 89%) quickly followed by chills, nausea, vomiting, headache, and hyperthermia (40.3°C) without signs or symptoms of transfusion-related acute lung injury or transfusion-associated circulatory overload. Transfusion-transmitted bacterial infection (TTBI) was suspected and the transfusion was stopped. Blood samples were taken for culture and empiric antibiotic therapy was immediately administered (piperacillin/tazobactam, amikacin, and vancomycin). On Day 1, 20 hours after transfusion, the patient displayed acute desaturation and chest x-rays revealed pulmonary interstitial syndrome. The patient was intubated and ventilated from the next day (Day 2). The patient then developed severe acute respiratory distress syndrome and extracorporeal circulatory support was initiated. PLT transfusion support was provided regularly. The neurologic progression was critical and the patient died on Day 7.

Donor investigations

The APC was collected on February 16 at 3:00 PM from an 80-minute apheresis PLT and plasma donation with a cell separator using the manufacturer's universal PLT protocol (MCS+, Haemonetics).[2] Skin decontamination involved a four-step procedure with povidone iodine/ethanol. The apheresis process took place without any reported problem. The APC was delivered on Day 0 by the hospital transfusion service after control of the swirling. The APC was transfused on February 18 at 12:00 PM, 45 hours after donation. No anomaly in the procedure of conservation of the product before the transfusion was noted.

The donor was a 19-year-old woman. She had already given blood three times in the previous year. No infectious symptom was reported during the medical interview before the donation, and no postdonation information was received. On the day of the donation, her WBC count was 5.83×10^9/L.

On Day 2, the blood center called the donor and she confirmed not having any urinary or digestive symptoms before or after the donation. She came back on Day 8 to undergo additional tests. Physical examination was normal. In view of the bacteriologic results for the patient (see below) the donor was referred to an ear, nose, and throat service. No existing nose or sinus disorders were found; examination of the nasal cavities and sinuses was normal and there was no visible evidence of infection. Complementary explorations showed no abnormalities (dental panoramic x-ray and sinus CT scan).

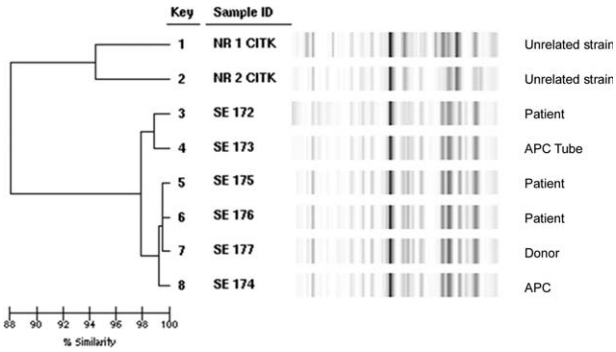

Fig. 1. Amplification profile of *C. koseri* isolates by rep-PCR (Diversilab). CITK = *C. koseri*; ID = identity; NR = not related.

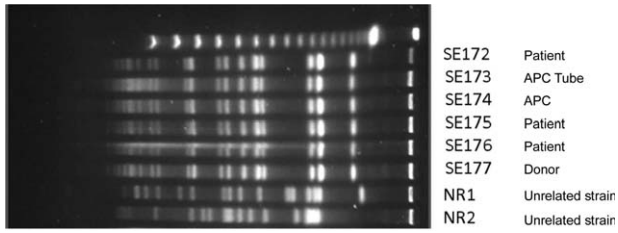

Fig. 2. *C. koseri* DNA profiles by pulsed-field gel-electrophoresis.

Bacteriological investigations

Cultures of patient blood sampled on Days 0, 1, and 2 were all positive for *Citrobacter koseri*.[3] *C. koseri* was isolated from APC culture 12 hours after the event from the few milliliters of APC remaining in the PLT bag.

Cultures of samples of donor blood, stool, urine, the skin of the inside of the elbow at the point of needle insertion, and ear were all negative for *C. koseri* but a nasal sample was positive for *C. koseri*. All *C. koseri* isolates had the same antimicrobial susceptibility pattern as wild-type strains.

The *C. koseri* isolates were genotyped using pulsed-field gel-electrophoresis of DNA macrorestriction (*Xba*I) and repetitive sequence-based polymerase chain reaction (rep-PCR) as previously described.[4] All the isolates had identical patterns on pulsed-field gel-electrophoresis and had more than 95% of similarity by rep-PCR. The isolated bacteria were, therefore, all of the same strain (Figs. 1 and 2).

DISCUSSION

Although TTBI is a rare adverse event, it is the highest infectious risk,[5] especially after PLT concentrate transfusion. Numerous measures are used to reduce contamination of blood products:[6,7] selection of donors, choice of medical devices for blood donation, skin asepsis procedures, rejection of the first 30 mL of donated blood donor,

WBC counting on the day of the donation, prevention of bacterial proliferation by removing WBCs, ensuring high-quality storage of donated blood, blood product visual examination (swirling), and collection of information after donation. However, as in our case, even if these measures are implemented, there are still serious accidents. In France, the residual risk of TTBI, after consistently decreasing, is stable at a low level: 0.19 per 100,000 blood products transfused with around one fatal event each year. Further improvement of transfusion safety, to reduce this risk, may require new measures, such as bacterial detection or inactivation of blood components, for example, by the Intercept method that is not currently used in our center. An analysis of cost-effectiveness is necessary before such measures can be implemented. The bacteria responsible for TTBI mostly come from the bacterial flora of the skin;[5] however, some are from transient asymptomatic bacteremia or asymptomatic urinary tract or digestive infection.[3]

C. koseri is an Enterobacteriaceae species usually found in the intestinal tracts of animals and humans and in soil and water.[3] In this case, the site from which it was isolated is unusual: the *Citrobacter* strain was isolated 1 week after the blood donation from the donor's nostril, but nowhere else, and no anatomic abnormality of the ear, nose, and throat was detected. It was not possible to determine why and how this strain was present at this site and no measures exist to prevent infection of blood products donated by individuals with such infections. The bacteria appeared to be sensitive to the prophylactic antibiotics administered to the patient, so it is plausible that the death was due to endotoxin shock.

In conclusion, this fatal accident, involving an Enterobacteriaceae isolate, with an unusual localization in an asymptomatic donor and 2-day-old transfused APC, was not associated with any dysfunction in the transfusion chain. The potential value of the implementation of complementary measures to improve transfusion safety in terms of bacteriologic contamination of blood products, and in particular detection and/or bacteriologic inactivation,[6] should be considered.

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LH collected the data and wrote the case report; SM collected the data; SB realized the microbiologic studies and comparisons of bacteria; LR supported the donor in the blood center; NAO, MB, and DA participated in the treatment of the patient; AB participated in data collection; MS wrote the case report; TBP and BP participated in the microbiologic study; and PB supervised the enquiry and provided critical revision of the manuscript.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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