Septic Transfusion Reactions Despite Implementation of Methods to Reduce Bacterial Contamination

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Reports of screening breakthroughs

- CDC has been made aware of septic transfusion reactions that occurred after receipt of platelets screened for bacterial contamination
  - FDA fatality reports
  - Requests for consultation or testing
- Three case reports illustrate some of the challenges of platelet screening.

Case I- Clinical Summary

- 74 year old patient with leukemia on weekly platelet transfusions.
- Received 5 unit irradiated pool on 10/30/04 as an outpatient.
- No evidence of sepsis during or immediately after transfusion.

Case I- Clinical Summary

- Patient became ill on the ride home
  - Taken to a hospital
  - Found hypotensive and admitted
- Blood cultures grew *Staphylococcus aureus.*
- Patient died 21 days after hospital admission.

Case I- Microbiology Summary

- The 5 empty donor unit bags were cultured, and 2 of 5 grew *S. aureus.*
- *S. aureus* isolates from the patient and bags were genetically identical by molecular typing (PFGE).
- Co-components recalled
  - One released RBC cultured negative
  - Donor follow-up unremarkable according to blood center

Case I- Platelet Summary

- Of the five units in the pool, the oldest unit was four days old.
- Of the two contaminated donor units
  - Both two days old
  - Were the first two units pooled via a common spiking device
- Unit was pooled and irradiated within three hours of transfusion.

Case I- Screening Summary

- Facility uses pH test strips for screening.
- Test strips are regularly validated using a pH meter.
- If pH is <6.4, the unit is rejected.
- Actual pH is not recorded, only a pass/fail determination.
- The implicated unit passed these approved screening measures.

Case II- Clinical Summary

- 79 year old patient received a “jumbo” (480 cc) plateletpheresis unit for thromobocytopenia following coronary artery bypass surgery.
- About one hour post transfusion, patient developed shortness of breath, chills and fever to 39.4^{o}C.

Case II- Clinical Summary

- Following the transfusion, the patient developed multiple thrombotic events and died 27 hours later.
- Blood cultures from two sites grew a coagulase negative Staphylococci, later identified as *S. lugdunensis.*

Case II- Microbiology Summary

- Gram stain of material in the platelet bag revealed gram positive cocci and cultures of the bag grew *S. lugdunensis* in 8 hours.
- Isolates from the patient and bag were genetically identical by molecular typing (PFGE).

Case II- Platelet Summary

- The unit was 5 days old at transfusion.
- Donor history being gathered.

Case II- Screening Summary

- Apheresis platelets held for 24 hours before screening.
- After mixing, 4mL aliquot removed from the bag via a sterile connection.
- Aliquot is inoculated into one aerobic BacTAlert bottle.
- Incubator reads bottles every 10 minutes for length of product storage.

Case II- Screening Summary

- Screening cultures incubated for minimum of 12 hours before release.
- The sample from this unit was negative on day 5 (transfusion day).
- The blood culture bottle, after 10 days of incubation, was sent to CDC and retested
  - No organisms identified by culture or gram stain

Case III- Clinical Summary

- 700 gm premature newborn who received 2 doses of a single donor apheresis platelet unit, 24 hours apart.
- Several hours after the 1st transfusion, the baby's condition began deteriorating with hypotension and respiratory distress.

Case III- Clinical Summary

- Blood cultures of the recipient were negative (on broad spectrum antimicrobials).
- Gram negative rods were seen on a peripheral blood smear.
- Recipient died about 72 hours after 1st transfusion with symptoms of sepsis.

Case III- Platelet Summary

- The 1st aliquot was transfused after 3 days of storage.
- The 2nd aliquot was transfused after 4 days of storage.
- Donor investigation is pending.

Case III- Screening Summary

- The unit was held for 24 hours before screening.
- A 1 mL sample was taken from the bag (i.e., first aliquot), and 0.1 mL was placed onto blood agar solid media.
- Culture was negative at 24 hours, and the unit was released.

Case III- Screening Summary

- As part of QC, just prior to release of the 1st dose, an additional 1 ml was taken from the unit (i.e., second aliquot) and cultured on solid media.
- The second aliquot grew *Serratia marcescens*, but both of the unit's doses had been transfused by the time these results were known.

Case III- Microbiology Summary

- When re-cultured, the unit bag which held both doses grew *Serratia marcescens.*
- A re-culture of the remainder of the first aliquot using broth filtration did not grow the organism (estimated sensitivity, ~2 cfu/ml).
- pH of the unit bag was **7.3.**

Potential explanations for screening breakthroughs

- Clerical and handling:
  - Clerical errors
    - Mis-match of the unit tested and the report
    - Failure to actually test the unit
  - Contamination occurs after testing, (during storage and handling of the unit)

Potential explanations for screening breakthroughs

- Methodological:
  - Contamination is below limit of detection of the culture or other method.
    - Blood cultures are reported to have very low limits of detection (<10 organisms per mL), but data are based on use of two blood culture bottles at 8-10 ml each with incubation for >5 days.
    - Impact of reduced volume and shortened time?
  - pH and other metabolic indicators pose additional challenges due to lack of standardization, including use of generally accepted cutoffs.

Interdictions

- Expect >100 true positives upon screening per year.
- In 2004, some of positive results from screening of public health interest and/or clinical relevance:
- Gram positive organisms
  - Staphylococcus spp.(coagulase positive and negative)
    - *S. epidermidis* and other coagulase neg
    - *S. aureus* (reported osteomyelitis)
  - Streptococcus spp.(alpha and beta hemolytic)
    - Groups B, C, D, G various species
    - *S. bovis* (reported occult colon CA)
  - *Bacillus* spp.
  - *Listeria monocytogenes* (two different donor centers)
- Gram negative organisms
  - Enterobacteriaceae (e.g., *Serratia, Klebsiella, E. coli*)

For the Future

- AABB Standard has been followed by guidance for members
  - Case definitions (e.g., true positives) to aid QC and reporting consistency
  - Work-up of suspected contaminated units, particularly false negatives or “late positives”
  - Algorithms for organisms clinically relevant and those of public health significance
- National data collection and monitoring would be useful.

Conclusions

- Implementation of the AABB standard has resulted in many interdictions of bacterially contaminated platelet transfusions.
- Methodologies need to be evaluated in clinical setting with current “standard practice”, in addition to laboratory simulation (e.g., spiking studies).
  - pH and culture media (liquid and solid) have been associated with false negatives.
- Investigation of breakthrough infections should be used to collect data to improve detection methods.