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Detection of Enterotoxin Gene Cluster in *Staphylococcus epidermidis* Recovered from Neonatal Liver Abscess

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Introduction

- Neonatal pyogenic liver abscesses are rare
- Potential routes of hepatic infection include: portal vein, biliary ducts, hepatic artery during sepsis, or direct spread from infected contiguous structures
- Risk factors may include bloodstream infection, abdominal surgery, umbilical vein catheterization, total parenteral nutrition, necrotizing enterocolitis, and/or immune deficiencies
- More common in premature infants at present
- Variety of etiologic agents for neonatal liver abscess: *Staphylococcus aureus* (methicillin-susceptible and resistant), coagulase-negative staphylococci (CONS), streptococci, *Escherichia coli*, *Klebsiella*, *Pseudomonas*, *Enterobacter*, *Serratia*, and *Candida*
- Umbilical stump and catheter exit site hub often colonized with CONS
- CONS colonize nearly all human skin and are often considered contaminants when recovered from blood cultures and may be dismissed as non-pathogens when isolated from tissues and other body fluids
- CONS, including *Staphylococcus epidermidis*, have been found to harbor genes that encode for adhesion factors and exotoxins, among others
- Staphylococcal superantigens are exotoxins produced by *S. aureus* strains which contribute to the pathology of various serious diseases such as toxic shock syndrome, infective endocarditis, and other conditions such as Kawasaki disease and atopic dermatitis; some have been identified in CONS, including *S. epidermidis*
- We describe a premature newborn with hepatic abscess from whom a *S. epidermidis* strain was isolated that harbored multiple superantigen genes

Case Description

- Male infant delivered via Cesarean section at 29 weeks gestation with a birth weight of 900 g
- Intubated at birth, umbilical vein catheter (UVC) placed, and total parenteral nutrition (TPN) started
- Echocardiogram on day 5 of life showed mild heart dilation, atrial septal defect with left-to-right shunt, and a large patent ductus arteriosus (treated with indomethacin)
- UVC removed on day 7 because it was noted to be in the liver
- Abdomen was distended on day 10 of life
- Abdominal ultrasound (US) on day 12 of life showed 3 separate hepatic abscesses, the largest of which was 2.3 x 1.6 x 1.9 cm (Figure); his white blood cell count was 21.4 bil/L with an absolute neutrophil count of 9.83 bil/L, C-reactive protein 88 mg/L, albumin 2 g/dL, and normal AST and ALT
- Intravenous vancomycin, cefepime, and metronidazole were started after a blood culture was obtained (sterile)
- On day 14 of life, he underwent US-guided percutaneous aspiration of the larger hepatic abscess with drainage of 3 mL of pus; a pigtail catheter was left in place
- Antibiotics were changed to intravenous piperacillin-tazobactam and vancomycin post drainage

Case Description (cont.)

- The bacterial culture of drained pus grew *Staphylococcus epidermidis* that was resistant to oxacillin and erythromycin, but susceptible to clindamycin (no inducible clindamycin resistance *in vitro*), levofloxacin, tetracycline, trimethoprim-sulfamethoxazole, and vancomycin; anaerobes were not recovered
- On day 17 of life, the antibiotic regimen was changed to oral clindamycin and he was treated for a total of 14 days after the drainage procedure
- Serial hepatic US examinations through the first 5 months of life showed gradual resolution with residual echogenicities and calcifications

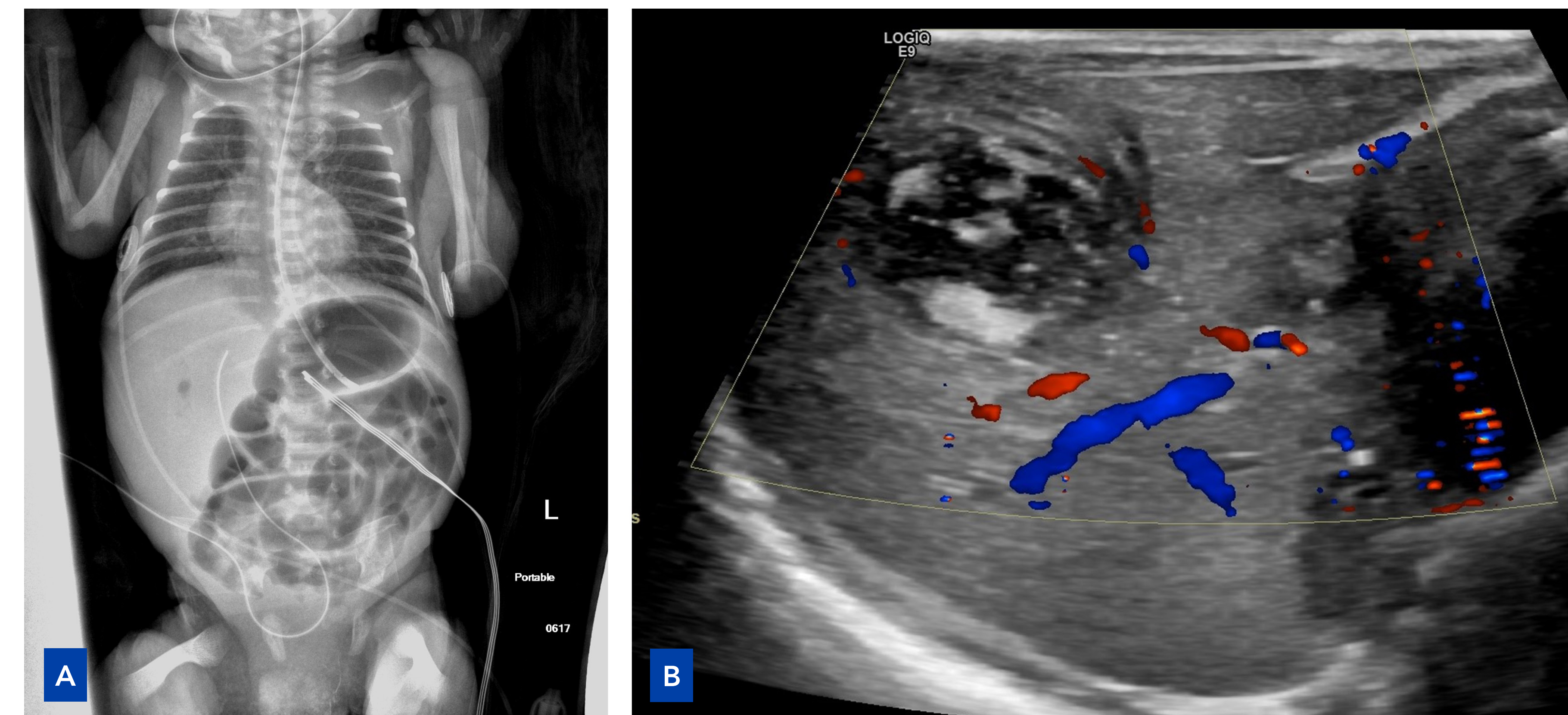
Methods

The *Staphylococcus epidermidis* isolate was tested for the following superantigen genes by polymerase chain reaction (PCR): toxin shock syndrome (TSS) toxin-1, staphylococcal enterotoxins (SEs) A, B, C, D, E, and G, and staphylococcal enterotoxin-like (SEL) superantigens, I, K, L, M, N, O, P, Q, U, and X with PCR primers specific for each superantigen.

Results

- The *S. epidermidis* isolate was positive for the enterotoxin gene cluster of six superantigens: SEG, SEL-I, M, N, O, and U
- This represents the first demonstration of this group of six superantigen genes in CONS
- When these genes are present, five of the six superantigens are produced in low amounts, and are considered colonization factors
- SEL-U, which is highly related to SEC, is one of the major causes of non-menstrual toxic shock syndrome

Figure. (A) Umbilical venous catheter tip overlying the liver and a small amount of extraluminal gas in the right upper quadrant. (B) Sonographic image of a heterogeneous avascular intrahepatic fluid collection.



Discussion

- Significance of CONS isolated from clinical specimens is changing with the recognition that they are a heterogeneous group with many harboring a variety of virulence factors that can cause tissue injury for humans.
- Our infant had multiple risk factors for hepatic abscess formation such as UVC migrating into the liver, TPN administration through the UVC, and immaturity of the immune system.
- The source of *S. epidermidis* is likely the umbilical stump and surrounding skin, with migration to the liver parenchyma along the UVC.
- Identification of known staphylococcal virulence factor genes in CONS isolates can help determine whether they are pathogenic in specific clinical settings, thereby allowing better informed antibiotic treatment decisions.
- Imaging-guided percutaneous drainage of hepatic abscesses in newborns may obviate the need for more invasive surgical procedures.
- Drainage of hepatic abscesses can allow shorter durations of antimicrobial therapy and the use of an oral agent instead of prolonged intravenous medication administration.

Conclusions

The group of 6 staphylococcal superantigens, especially SEL-U which is highly related to SEC, is likely to have contributed to the development of *Staphylococcus epidermidis* liver abscesses in this premature neonate. Recovery of *S. epidermidis* from an abscess cavity should not be dismissed as a contaminant.

References

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