Coagulase Negative Staphylococcal Sepsis With Upper Extremity Gangrene And Shock In A Premature Infant: An Unusual Complication Of A Peripheral Intravenous Catheter

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Citation

Abstract
Upper extremity gangrene following infiltration of a peripheral intravenous catheter (PIV) in a 24-week premature infant with coagulase negative staphylococcal (CONS) sepsis is reported. Although CONS are the most common cause of nosocomial infection in premature infants, septic gangrene from a PIV is an unusual complication that we have not found described previously.

ABBREVIATIONS
DOL Day of life UAC Umbilical artery catheter UVC Umbilical vein catheter PIV Peripheral intravenous catheter PDA Patent ductus arteriosus CONS Coagulase negative staphylococci WBC White blood cell count ANC Absolute neutrophil count LBW Low birth weight (<2500 grams) VLBW Very low birth weight (<1500 grams) ELBW Extremely low birth weight (<1000 grams)

CASE REPORT
This male infant, the 795 gram product of a 24-5/7 weeks gestation, was delivered vaginally and had Apgar scores of 4 and 7 at 1 and 5 minutes, respectively. An UAC was placed with the tip at T7 and remained in place throughout life. Attempts to place an UVC were unsuccessful. The initial WBC was 7.5 k/µl with 15% neutrophils, 2 % bands and ANC 1275 /µl. Platelets were 165 k/µl. Physical exam was remarkable for an extremely premature infant with thin gelatinous skin and fused eyelids. The initial sepsis evaluation with a blood culture was negative. He received three doses of indomethacin, and a follow up cardiac echogram on DOL 3 confirmed a closed ductus arteriosus. On DOL 3 the infant developed thrombocytopenia with platelets decreasing to as low as 80 k/µl. A heparin-locked PIV, initially placed on the dorsal surface of the left wrist at birth, infiltrated on DOL 4 with subsequent local swelling. It remained in place and was managed expectantly. The PIV had previously been used for insulin, indomethacin and a packed red blood cell transfusion. The infant was started on vancomycin and cefotaxime on DOL 5 due to a left shift on the CBC. On DOL 6, a 2.5 x 2.5 cm black eschar was noted at the left wrist, at the site of the PIV infiltration. Physical exam revealed pink, adequately perfused digits and a good radial pulse. The PIV was discontinued. A repeat blood culture on DOL 7 rapidly grew out CONS in 1/1 bottle. Clindamycin was added to the antibiotic regimen pending sensitivities. On DOL 8 the WBC was 5.0 k/µl with 1% neutrophils, 13% bands and ANC 700 /µl. A third blood culture grew out CONS in 1/1 bottle. The eschar had now increased in size to 5 x 2.5 cm and there was purple discoloration and edema of the wrist, as well as poor pulses (Figure 1).
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Figure 1
Figure 1: Photograph of the left forearm of the infant upon admission (DOL 8). There is marked discoloration and edema extending from the wrist towards the antecubital fossa. The hand is discolored and edematous as well.

The infant was transferred to the University of California Medical Center. Upon admission, the WBC was 4.7 k/µl with 1% neutrophils, 1% bands and ANC 94 /µl. Platelets were 134 k/µl. Initially the patient was thought to have fair circulation to the left hand. Five hours later, he rapidly deteriorated with hypotension, progressive purpura of the left wrist with no capillary circulation being present in the hand, and a profound and progressive metabolic acidosis (Base deficit as high as 26). The infant did not respond to resuscitation and expired.

DISCUSSION
The key elements in this case were the placement of umbilical lines on DOL 1, the infiltrated PIV on DOL 4 and a positive blood culture for CONS on DOL 7. There were clinical signs of sepsis by DOL 3 (thrombocytopenia), DOL 5 (left shift) and DOL 8 (falling WBC-counts and development of neutropenia). At the same time, there was progressive gangrene of the left upper extremity.

Limb gangrene most often affects the lower extremity and is often related to vascular catheters. The incidence of thrombosis with a high UAC is 24%. Even in the presence of a high UAC, thromboembolic complications to the upper extremities are rare. An embolus from the previously disturbed umbilical vein, that reached the arterial circulation across a patent foramen ovale is also less likely, since signs of sepsis did not develop until DOL 3. The gut itself may represent another potential focus. Scheifele et al. showed that many gut derived CONS isolates produce a potent cytotoxin, capable of causing necrosis. A more plausible scenario is that bacteremia occurred secondary to the indwelling UAC or to the PIV itself, with seeding of the infiltration site, perhaps serving as a secondary focus for the infection.

Compartment pressures and arterial doppler flow were never performed, but it is conceivable that arterial insufficiency developed secondary to a compartment syndrome, since edema and discoloration preceded the development of poor arterial pulses. Given the data from Cronin et al., we cannot exclude the possibility that the PIV was the port of entry for the infection, where it would have functioned as the primary focus. Regardless of the etiology, septic gangrene in the overall incidence of CONS bacteremia, i.e. isolation of the bacteria from 2/2 bottles of a blood culture set, is 3.4-4.8 % (9,10). More than two thirds of these babies are LBW. The incidence of sepsis if a positive blood culture is present ranges from 26-78.3% with the mortality approximating 15-17%. Risk factors for CONS sepsis in VLBW infants include the use of umbilical catheters, parenteral nutrition, early antibiotic treatment and the presence of a PDA.11 Landers et al. prospectively studied 357 umbilical catheters. Catheter related sepsis occurred in 3-5% of the patients. In 48% of the cases, CONS were the responsible pathogen. Cronin et al. studied the incidence of catheter colonization, the relationship to the type of catheter and duration of use. Of PIVs in place for <3 days, 11.6% were colonized compared to 30.8% of PIVs in place >3 days. The isolated organisms were CONS in 79% of the cases.

Although small, the data are striking: 7/11 blood stream infections were catheter related; CONS were the offender in 5 of these cases; 6/7 infections had a PIV (with colonized tip) in place within the last 4 days, as compared to only 2/6 which had a central line in place concomitantly. Having a PIV in place >3 days at the same site is an independent risk factor for bacteremia in general.

Our patient had several risk factors for CONS sepsis and there are different possible scenarios for the etiology of the gangrene. Thromboembolism from the UAC to the upper extremity seems unlikely given the much higher propensity for lower extremity thromboembolic complications. An embolus from the previously disturbed umbilical vein, that reached the arterial circulation across a patent foramen ovale is also less likely, since signs of sepsis did not develop until DOL 3. The gut itself may represent another potential primary focus. Scheifele et al. showed that many gut derived CONS isolates produce a potent cytotoxin, capable of causing necrosis. A more plausible scenario is that bacteremia occurred secondary to the indwelling UAC or to the PIV itself, with seeding of the infiltration site, perhaps serving as a secondary focus for the infection.

CONS are the most common cause of nosocomial infection in the intensive care nursery. They are responsible for 50% of all neonatal blood stream infections, with the incidence inversely correlating with birth weight. The incidence of CONS sepsis in VLBW infants is as high as 17%. The
upper extremity is an unusual morbidity even in the critically ill neonate.

Limb saving fasciotomy has been described in stable, term or near term neonates with apparently good outcome. Ibrahim et al. recently described Staphylococcus Aureus sepsis complicated by popliteal vein thrombosis and compartment syndrome in a 30 week VLBW infant. We are not aware of any reports that describe the use of fasciotomy in an ELBW and critically ill infant. Given the overwhelming sepsis, any surgical intervention would be extremely risky and of uncertain benefit.

Since an autopsy was not performed, we cannot prove that the gangrene was caused by CONS. We therefore acknowledge that our report is speculative. However, the premature and septic ELBW infant with arterial insufficiency due to catheter complications, presents a unique problem to the practitioner. We hope that this unusual case will stimulate other clinicians with similar experiences to scrutinize any focal PIV infiltrates to prevent the progression we experienced.

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