UNILATERAL SHOULDER SWELLING IN A PRETERM NEONATE

CASE PRESENTATION

A former 27 week gestation, 1090 gram birth weight Hispanic female infant was born by caesarean section because of transverse lie and preterm labor. The mother had received no prenatal care. The infant was treated at the time of delivery with Survanta™ for hyaline membrane disease. Umbilical artery and vein catheters were placed at birth and discontinued on day of life (DOL) five and seven, respectively. On DOL six, a peripherally inserted central catheter (PICC) was placed into the right upper extremity without complications. The infant’s neonatal course was complicated by bacteremia due to coagulase negative Staphylococcus (CONS) on DOL 18. The PICC line was removed on that day because of infiltration of fluid into the soft tissues at the insertion site in the antecubital fossa. Urine and CSF cultures were sterile. The patient completed a two week course of intravenous vancomycin therapy on DOL 33.

The patient was clinically stable receiving minimal ventilatory support until DOL 33 when she was noted to have a lump over her right clavicle and pain upon movement of her right shoulder. With the exception of several episodes of apnea and bradycardia, there were no other changes in the infant’s clinical status. There was no history of recent or remote trauma. The physical examination revealed that the temperature, blood pressure, and respiratory rate were within normal parameters. The anterior fontanelle was soft and flat, the neck was supple, and there was no adenopathy. The heart, lungs, and abdomen examinations were normal. The right shoulder was minimally swollen and erythematous, but there was full range of motion about this joint. There was a 2.5 by 3.0 centimeter nonmobile mass over the medial right clavicle that was erythematous, warm, and markedly tender to palpation. The remainder of the extremity exam
was normal.

The white blood cell (WBC) count was 16,800/mm³ (30% neutrophils, 50% lymphocytes, 12% monocytes, 5% eosinophils). The hemoglobin was 8.5 g/dL, the hematocrit 25.1%, and platelet count 323,000/mm³. The serum electrolyte concentrations were within normal limits. The erythrocyte sedimentation rate (ESR) was 23 mm/hr (normal value = 0-20) and the C-reactive protein was 0.48 mg/dL (normal value = <1.0). Radiographic examination of the right shoulder revealed absence of the proximal third of the right clavicle associated with an osteolytic process and possible fracture (Figure 1).

Intravenous vancomycin (15 mg/kg every 8 hours) was empirically initiated. Additional diagnostic studies included daily blood cultures until DOL 36 which were sterile, an MRI of the clavicle on DOL 37 which showed an area of nodular inflammation limited in detail by motion artifact, and an ultrasound with doppler studies of the right subclavian vein which revealed a patent vessel. On DOL 51 (day 13 into vancomycin therapy), open biopsy of the right clavicle was performed.

What is your diagnosis?

Infection? Infusion-related “trauma”? Tumor?
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The differential diagnosis in a preterm neonate hospitalized since birth who presents with unilateral shoulder swelling and pain includes fracture, osteomyelitis, superficial cellulitis, osteitis, subcutaneous abscess and malignancy. Bony changes similar to those of osteomyelitis have been described in infants with congenital tumors and leukemia. Additional noninfectious causes that can show bone destruction and periosteal reaction include trauma, Caffey’s disease, prostaglandin E infusion, and extravasation of calcium gluconate at the infusion site. Developmental anomalies of the clavicle such as pseudoarthrosis and synovial cysts can present with a focal mass or deformity, but pain usually is absent.

Initially, fracture and osteomyelitis were considered as the primary etiologies for this infant’s focal findings. An important diagnostic clue was found on the chest radiograph from DOL 17; the distal tip of the right upper extremity PICC terminated at the mid-clavicular line, anatomically adjacent to the site of the future clavicular mass. The possibility of an intravascular catheter-associated osteomyelitis was considered and a bone biopsy was requested. A Gram stain of the biopsy specimen revealed rare white blood cells and no organisms. Histologic examination showed extensive areas of acute inflammation and necrosis, with a fibrotic reaction confirming the suspicion for osteomyelitis (Figure 2). The biopsy culture grew CONS only from the broth media. This isolate was susceptible to vancomycin, ciprofloxacin, gentamicin, trimethoprim-sulfamethoxazole, rifampin, and tetracycline. This susceptibility pattern was identical to the CONS isolate from the blood during the initial sepsis episode on DOL 18. After 72 hours of vancomycin therapy, the swelling and tenderness of the right clavicular mass began to resolve. The infant received six weeks of vancomycin. There were no recurrences of her signs of infection throughout the remainder of the hospital stay. A follow-up radiograph taken at
5 months of age showed regeneration of the right clavicle with only minimal dysmorphism (Figure 3).

Neonatal osteomyelitis is uncommon, with a reported incidence of 1 to 3 cases per 1000 admissions to intensive care nurseries.\(^1\) Hematogenous origin during the course of neonatal septicemia is the most common route for microorganisms to reach the skeletal structures.\(^1-4\) Long bones, such as the femur and humerus, commonly are most affected, with only about 2% of reported cases involving the clavicle.\(^2\) In long bones, the adjacent joint is routinely involved whereas this may not be true for tubular bones. The most frequent pathogen in neonates with osteomyelitis is \textit{Staphylococcus aureus}.\(^1-5\) Less frequently isolated organisms include \textit{Streptococcus agalactiae, Escherichia coli, Klebsiella, Proteus, Enterobacter,} and \textit{Candida} species.

The use of intravascular catheters has been associated with osteomyelitis in neonates.\(^1-3,5\) It is believed that septic embolization from catheter tip thrombi together with local hypoxia from partial occlusion of the vessels by the catheter are key components in the pathogenesis of bone infections.\(^2\) These catheters may become colonized either initially as they are inserted or subsequently as a result of a transient bacteremia. In this patient, infiltration of the PICC line on DOL 18 likely led to extravasation of fluid out of the vessel resulting in surrounding tissue damage from localized pressure and chemical irritation. Concurrent sepsis further compromised venous integrity by capillary leakage at the site and allowed a passageway for the bacteria to invade the underlying soft tissue spaces and eventually the bone itself.

Although CONS is an uncommon cause of neonatal osteomyelitis, there were multiple factors in our patient that are known to increase the likelihood of developing CONS infection and subsequent complications. Intravascular devices are associated with almost one-half of
CONS infections. Prolonged total parenteral nutrition, for the same reason, represents an increased risk for device-associated osteomyelitis, and intravenous lipid administration and CONS bacteremia are strongly associated. Prematurity and low birth weight also are risk factors both for CONS bacteremia and for osteomyelitis.

The diagnosis of neonatal osteomyelitis can be challenging. The majority of neonates with osteomyelitis present with little or no evidence of infection except for localized swelling, decreased range of motion, and tenderness. Systemic manifestations generally are absent. Neonates with indolent illness are feeding well and gaining weight. Involvement of multiple sites occurs in less than half of reported cases, and likely represents a more severe septicemia upon initial presentation. Laboratory evaluation often is not helpful. As in this patient, hematologic findings such as white blood cell count, platelet count, and ESR often are within normal limits. Blood cultures identify the etiologic agent only in approximately 25% of cases. A lumbar puncture should be performed because osteomyelitis usually results from bacteremia and evaluation of other sites of infection is necessary to define the extent of disease. This is especially true for agents other than Staphylococcus aureus since this organism is an extremely rare cause of CNS infection. Unlike older infants and children, radiographic evidence of osteomyelitis in neonates can be evident earlier, usually within seven to ten days of initial infection.

Successful treatment depends on a prompt clinical diagnosis and identification of the causative agent. When blood cultures are sterile, a bone biopsy should be performed. Initial antimicrobial therapy should be guided by Gram stain of aspirated material, or by a presumptive bacteriologic diagnosis. Indwelling catheters should be removed promptly when feasible. Surgical drainage is indicated when there is a significant collection of purulent material in the
soft tissues, subperiosteal space, metaphysis or adjacent joint. Because of the possibility of that
*S. aureus* may be methicillin-resistant, intravenous vancomycin was initiated as empiric therapy.
The optimal duration of therapy in neonates is unclear. A 3 to 6 week course of intravenous
treatment is recommended, and the exact duration is based on the patient’s clinical response,
improvement in radiographic findings, and the return of the ESR, if elevated, to normal.

This case illustrates the importance of CONS as a possible cause of neonatal
osteomyelitis, especially in the setting of an intravascular catheter with fluid extravasation.
When blood cultures are sterile, bone biopsy is necessary to identify the etiologic agent and to
select appropriate therapy.
REFERENCES


FIGURE 1. Plain radiograph of the chest demonstrating an osteolytic lesion (arrow) with absence of the proximal third of the right clavicle.
FIGURE 2. Histological specimen from the right clavicle demonstrating acute inflammation with numerous polymorphonuclear cells (A), necrosis (B), and nonviable bone (C), consistent with acute osteomyelitis.
FIGURE 3. Plain radiograph taken at 5 months of life showing regeneration of the right clavicle.