January 2014 Case Study

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CC:
Knee pain and fever

HPI:
A previously healthy 14 year-old cross country runner initially developed right knee pain while at cross country camp four days prior to presentation. Over the next three days the pain worsened and he developed daily fever, body aches, shortness of breath, pleurisy, and diarrhea. At that time he was referred to the local emergency department where he was found to have a right middle lobe pneumonia treated with azithromycin and ceftriaxone. Shortly after admission, however, he developed increasing respiratory distress and hypotension. He was fluid resuscitated, started on vancomycin, epinephrine and dopamine and emergently transferred to our facility for further management.

Physical Examination:
Vital signs: Temp: 97.7, HR: 156, BP: 78/58, RR: 47, and SaO2: 94% on 3L 100% O2. Physical exam reveals a well-developed, ill-appearing adolescent male in acute distress with intercostal retractions and crackles over his right lung fields, diffuse abdominal tenderness with guarding and hypoactive bowel sounds, 1+ distal upper and lower extremity pulses, and tenderness, warmth, redness and swelling circumferentially over his right knee and proximal right calf without discrete areas of fluctuance or induration.

Differential Diagnosis:
Septic shock
Bacteremia
Tick-Borne Illness
Community-acquired Pneumonia
Osteomyelitis
Septic knee joint
Pyomyositis

Lab studies:
WBC 1.4, Hgb 12.6, Hct 37, Plts 82, Na 138, K 4.3, Cl 116, HCO3 15, BUN 26, Cr 1.61, glucose 141, Ca 7.0, CRP 16.9, ESR 10, INR >10.0, PTT >200.0, pH 7.14, CO2 63, lactate 7.1, and CPK 38464.

Blood cultures from the outside hospital and our facility ultimately grew methicillin-resistant Staphylococcus Aureus (MRSA) also resistant to erythromycin and levofloxacin, but sensitive to clindamycin, doxycycline, gentamicin, rifampin, trimethoprim-sulfamethoxazole, and vancomycin.
Imaging studies:

Chest x-ray demonstrated bilateral patchy infiltrates with pulmonary edema and small bilateral pleural effusions.

Right femur MRI demonstrated R femur osteomyelitis, periosteal abscesses, and pyomyositis.
Diagnosis:
Community-acquired MRSA pneumonia and sepsis secondary to right femoral osteomyelitis

Treatment:
In the emergency department, the patient initially required extensive fluid resuscitation, epinephrine, dopamine, and hydrocortisone for persistent hypotension. Once his blood pressure stabilized he was intubated and placed on mechanical ventilation. He continued on vancomycin and ceftriaxone, with clindamycin and doxycycline added shortly after presentation. He was transferred to the PICU and cannulated for extracorporeal membrane oxygenation. The following day he was started on dialysis for renal failure. After the blood culture results became available his antibiotic therapy was changed to vancomycin, daptomycin, and linezolid.

Outcome:
The patient’s initial PICU course was further complicated by subdural hemorrhage, left hemiparesis secondary to ischemic brain infarct, adult respiratory distress syndrome, bronchopleural fistula with persistent right hemopneumothorax, Klebsiella tracheitis, pericardial effusion, gastrointestinal bleeding, anemia, persistent lower extremity thrombi, persistent electrolyte derangements, and delirium. Over the following two months, however, he was decannulated from ECMO, weaned to room air, taken off dialysis, successfully initiated a PO diet, and slowly returned to his neurological baseline with minimal residual left upper extremity weakness. Repeat MRI 3 months after presentation demonstrated chronic osteomyelitis with areas of necrotic bone, improved circumferential myositis, and a small, residual subperiosteal distal femoral abscess that required further incision and drainage.

He was ultimately discharged from the hospital fifteen weeks after initial presentation to an inpatient rehabilitation facility. He has since returned home and repeat x-rays show chronic osteomyelitis and
continued new periosteal bone formation. He currently remains on a prolonged course of clindamycin monotherapy as well as digoxin, carvedilol, and enalapril for cardiac contractility and afterload reduction. He is ambulatory and has returned to school but is currently restricted from sports participation due to his chronic osteomyelitis and risk of pathologic fracture.

Discussion:

*Staphylococcus aureus* is a Gram-positive, coagulase-positive bacterium which has become increasingly prevalent in the community. Within ten years of the widespread use of penicillin, *S. aureus* developed resistance by producing penicillinase, an enzyme which cleaves the penicillin beta-lactam ring. A semisynthetic class of beta-lactam antibiotics (e.g. methicillin) was introduced in the 1960s to combat this resistance. Methicillin resistance developed in *S. aureus* through expression of an alternative penicillin-binding protein, which rendered the entire antibiotic class ineffective. While this resistant species was initially limited to health care settings, a separate strain emerged in the community in the 1990s.

CA-MRSA infection is a well-documented problem among athletic populations and colonization may be more common among athletes than the general population. In addition, nasal carriage rates in athletes have been shown to fluctuate during the season, increasing at times of highest athletic activity. Multiple outbreaks of skin and soft-tissue infection have been reported among athletes, primarily among team sports. In a retrospective review of 100 athletes, the Connecticut Department of Public Health identified 13 skin and soft tissue infections among football players, of which 6 had MRSA wound isolates and 2 required hospitalization. Lindenmayer investigated a 32-member high school wrestling team and found 6 MRSA infections, one of which resulted in hospitalization.

In contrast to the majority of case reports of CA-MRSA soft tissue infection among athletes, our adolescent patient exhibited CA-MRSA sepsis and necrotizing pneumonia, likely resulting from an underlying femoral osteomyelitis. Immunocompromised adults may be at the greatest risk for severe invasive CA-MRSA infections, but recent reports have identified the importance of CA-MRSA as a life-threatening pathogen among immunocompetent adolescents as well. Gonzalez et al presented a case series of 14 adolescents presenting with sepsis due to *S. aureus*, 12 of whom were found to have CA-MRSA. Thirteen patients (93%) had evidence of osteomyelitis, 6 (43%) had airspace disease, and 3 (21%) did not survive. Prior reports of osteomyelitis in athletes have identified infections of the calcaneus, vertebrae, and pubic symphysis, although the underlying pathogen is often not identified. A single recent case report described a presentation of acetabular osteomyelitis, septic arthritis, bacteremia and pneumonia secondary to CA-MRSA infection in a 12-year old Portuguese female athlete who ultimately recovered on linezolid monotherapy. This study represents the only other case of severe, invasive infection secondary to CA-MRSA osteomyelitis in an athlete that we are aware of.

Incision and drainage represents the definitive treatment for cutaneous MRSA infection, and may be sufficient for disease eradication in small, uncomplicated abscesses. Although current guidelines from the Infectious Diseases Society of America state that physicians can treat minor skin/soft-tissue infections empirically with beta-lactams, clinicians should choose from a different class when MRSA is suspected. Tetracyclines, quinolones, trimethoprim-sulfamethoxazole, rifampin, and clindamycin typically remain effective against MRSA infection. Severe infections often require hospitalization and treatment with vancomycin, linezolid, quinupristin-dalfopristin, tigecycline, teicoplanin, carbapenems, ceftobiprol, or daptomycin.

Emerging resistance patterns among CA-MRSA isolates are also important considerations in the selection of antibiotic therapy. While many CA-MRSA isolates are susceptible to clindamycin, others will
exhibit inducible resistance. Because a person’s treatment regimen does not necessarily need to include erythromycin for inducible resistance to clindamycin to occur in vivo, isolates found resistant erythromycin should be tested for inducible resistance to clindamycin test.\(^7\) Rifampin should not be used as monotherapy due to the rapid development of resistance, but combining rifampin with other antibiotics such as doxycycline or trimethoprim-sulfamethoxazole prevents the emergence of resistance. Similarly, quinolones typically provide adequate coverage but the rapid appearance of resistance precludes their use.\(^12\) Finally, because cellulitis and osteomyelitis can result from other organisms such as *Streptococcus* species, caution should be taken when considering the use of trimethoprim-sulfamethoxazole alone. In such cases, alternatives include the use of clindamycin or a combination of a beta-lactam plus trimethoprim-sulfamethoxazole.\(^14\)

Our patient was initially treated with vancomycin, daptomycin, and linezolid with resolution of bacteremia and gradual clinical improvement. The isolated strain of *S. aureus* ultimately demonstrated resistance to mexitillin, erythromycin and levofloxacin. Although prior reports among children with CA-MRSA have shown increasing rates of clindamycin resistance,\(^10\) the strain isolated in our patient was susceptible and did not demonstrate inducible resistance despite resistance to erythromycin. Once his susceptibility testing was available and his clinical status improved, he was ultimately transitioned to a prolonged course of clindamycin monotherapy with continued clinical improvement.

Whereas CA-MRSA in athletes typically presents as a relatively mild skin and soft tissue infection, we present a case of underlying MRSA femoral osteomyelitis in an adolescent athlete with subsequent progression to necrotizing pneumonia, septic shock, and multi-organ failure. Joint pain is a very common complaint among athletes, but concomitant fever without another obvious source should warrant further investigation as delay in treatment of invasive CA-MRSA infection can quickly result in life-threatening complications.

**References:**

2. Beigler


