Hematogenous Coagulase-Negative Staphylococcal Vertebral Osteomyelitis

Case Reports and Review of the Literature

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Abstract: Vertebral osteomyelitis (VO) is an infection that can lead to significant morbidity including paralysis and chronic pain. Identifying the responsible organism poses a challenge to the physician. Vertebral aspirates are often used to sample the infected region in an attempt to identify the responsible microbe when cultures of blood are negative or reveal an organism not typically associated with VO. To identify the clinical features of patients with coagulase-negative staphylococcal (CNS) VO, we reviewed 272 vertebral aspirates obtained at our institution over 5 years. We identified 7 patients with cultures that yielded CNS. All patients had indwelling intravascular lines or devices. All patients in whom blood cultures were performed had CNS isolated from cultures of blood. Four of the 7 patients had resolution of the infection with antibiotic treatment alone, and 2 patients required surgical intervention. Coagulase-negative Staphylococcus may be an etiologic pathogen when it is isolated from multiple cultures of blood in patients with VO and additional risk factors including an indwelling intravascular line or device. 

Key Words: MRSE, MSSE, coagulase-negative Staphylococcus, vertebral osteomyelitis

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BACKGROUND

Vertebral osteomyelitis (VO) is a debilitating infection. It is important to establish the etiological agent so that appropriate treatment can be administered. The most common organisms are coagulase-positive Staphylococcus (Staphylococcus aureus; 50%-60% of cases) followed by gram-negative bacilli and streptococci (20%-30%).1,2 Coagulase-negative staphylococci (Staphylococcus epidermidis) have been described as causing 15% to 20% of cases of hematogenous VO in several case series.1-4 Neither case series nor individual case reports3,4 have systematically examined the risk factors and clinical features of hematogenous coagulase-negative staphylococcal VO. We performed a retrospective chart review using electronic medical records to identify patients who had not undergone prior spinal surgical intervention and whose VO was diagnosed via needle aspiration/ biopsy. Our goal was to explore the risk factors and clinical characteristics of hematogenous non-post surgical coagulase-negative staphylococcal (CNS) VO.

Materials and Methods

A single-center retrospective chart review study was performed at the University of Michigan Medical Center. Potential cases were identified by review of a log maintained in the neuroradiology division of the radiology department of all patients who had undergone discal/vertebral needle aspiration/biopsies from February 2006 to July 2011. Patients who were found to have hematogenous VO caused by CNS were identified by performing a search of the clinical data repository using electronic medical record search engine (EMERSE).5 Search terms used included "staphylococcus," "coagulase negative staphylococcus," “Staphylococcus epidermidis,” “epidermidis,” “Staph...epti,” and “vertebral osteomyelitis.”

Cases of CNS VO were required to have the following: characteristic findings on magnetic resonance imaging (MRI) of the spine; coagulase-negative staphylococci isolated from a vertebral aspiration, and no previous surgical procedure involving vertebral bodies (including laminectomy or insertion of spinal hardware). Patients’ demographics and clinical information, including medical history, microbiological results, radiological studies, and treatment regimens, were then abstracted from the patients’ medical records. Statistical analysis consisted of standard means and standard deviation calculations using Excel. This study was approved by the University of Michigan Institutional Review Board (IRBME).

A systematic search of the literature on vertebral osteomyelitis was performed using the following sources: Medline database through PubMed and UM Medsearch (Ovid). The following syntax was used: “vertebral osteomyelitis, vertebral body osteomyelitis, Coagulase negative vertebral body osteomyelitis, or Staphylococcus epidermidis vertebral body osteomyelitis.”

CASE REPORTS

Case 1

A 63-year-old man (patient no. 6 in Table 1) with acute myelogenous leukemia had undergone an allogeneic stem cell transplant that was complicated by graft versus host disease. He developed a temperature of 100.2°F and lower back pain that progressively worsened over a 2-week period. On admission, the erythrocyte sedimentation rate (ESR) was 120 mm/h and the C-reactive protein (CRP) was 14 mg/dL. An MRI of the lumbar spine revealed changes consistent with osteomyelitis and discitis centered at the L5-S1 vertebral disc level without epidural spread or involvement of the thecal sac (ie, cauda equina). Twelve months previously, the patient had CNS isolated from cultures taken from both an Infusaport and from peripheral blood. No treatment was administered at that time, as the organisms identified in the blood cultures were thought to be contaminants. At the time of presentation, blood cultures drawn from his implanted chest Infusaport grew coagulase-negative Staphylococcus. Repeat blood cultures also yielded CNS both from the port and from peripheral blood.
Because of uncertainty about the causal role of the CNS blood isolate, a computed tomography (CT)-guided aspirate from the L5-S1 disc region was performed. Coagulase-negative Staphylococcus was isolated from cultures of this aspirate. The patient had no peripheral stigmata of endocarditis, and no valve vegetation was seen on a transthoracic echocardiogram. The Infusaport was removed, and the patient initially received vancomycin, to which he developed intolerance. Subsequently, daptomycin, 6 mg/kg, was administered for 12 weeks. At the conclusion of therapy, he reported significant improvement of the back pain, and there was a reduction in ESR and normalization of the L5-S1 disk region signal abnormality on a follow-up MRI.

Case 2

A 50-year-old man (patient no. 3 in Table 1) with Crohn’s disease presented with low back pain for 3 weeks. He was receiving total parenteral nutrition through a peripherally inserted central venous catheter (PICC) line because of short gut syndrome. This developed after a Whipple procedure, which had been performed to resect a gastrointestinal tumor. The ESR was elevated at 67 mm/h, and CRP was 2.3 mg/dL. An MRI demonstrated imaging findings consistent with osteomyelitis/discitis at the T8-T9 level (Fig. 1). He denied fever or chills. Coagulase-negative Staphylococcus was isolated from numerous sets of blood cultures drawn over a period of 3 days. The PICC line was removed, and culture of the catheter tip also yielded a CNS with a phenotype consistent with the blood isolates.

A CT-guided aspirate of the T8-T9 disk region was performed because of uncertainty about the significance of CNS isolated from cultures. Coagulase-negative Staphylococcus was also isolated from this aspirate. He was treated with intravenous vancomycin for 6 weeks followed by oral doxycycline and then Keflex for 6 months. A follow-up MRI showed development of mild anterior wedging of the T8 vertebral body with mild associated kyphotic deformity of this portion of the thoracic spine.

![FIGURE 1](image-url) Patient no. 3: Presenting sagittal fat-saturated T2-weighted MRI of the spine demonstrates end plate irregularity loss of intervertebral disc height and abnormal signal from the contiguous portions of the T8 and T9 vertebral bodies at the T8-T9 level consistent with discitis and osteomyelitis. These regions also demonstrated contrast enhancement (not shown).
(Fig. 2). However, his pain improved and the ESR and CRP returned to the normal range.

RESULTS

Of the 251 patients who underwent 272 vertebral biopsy procedures, 7 patients were identified with VO caused by CNS over the 5-year period of this study. No patient included in the study had previous surgery of the spine at the site of infection. The mean ± SD age of patients was 59 ± 8 years (range, 50–73 years). Six patients were white, and one was African American. The patients presented with a history of back pain ranging from 14 days to 4 months. One patient described symptoms of chills; otherwise, no patient had a documented temperature greater than 100.5°F. At the time of diagnosis, the ESR was elevated in all cases with an mean ± SD of 72 ± 27 mm/h. The C-reactive protein was similarly elevated in all cases with a mean ± SD of 6.8 ± 7.9 mg/dL. In all cases, spine MRI demonstrated changes consistent with discitis including abnormal discal and contiguous vertebral signal changes with varying degrees of enhancement. The MR scans did not show extension of inflammatory changes into the spinal canal or immediate paravertebral regions in any patient.

Blood cultures were performed in 6 of 7 patients before aspiration/biopsy; CNS was isolated from those blood cultures in each of the 6 patients. The duration of bacteremia ranged from 1 to 5 days. All abnormal disks/vertebra were identified in the thoracic or lumbar regions. One patient ultimately developed a paraspinal abscess. Cultures from percutaneous CT-guided disc/vertebral aspirates/biopsies yielded methicillin-sensitive CNS in 3 cases and methicillin-resistant CNS in 4 cases.

All patients had an indwelling intravascular device present but no evidence of cutaneous infection at the site of device insertion or elsewhere. Two patients were receiving hemodialysis through a central venous catheter; 2 others were receiving infusions through a PICC line. One patient each had a Hickman catheter, an implanted Infusaport, or a cardiac defibrillator. All patients had significant comorbidities, including cancer, renal failure, or diabetes, as listed in Table 1.

The duration of antimicrobial therapy ranged from 6 to 12 weeks. Four patients received vancomycin, and 2 patients were treated with daptomycin. One patient sequentially received cefazolin, vancomycin, and then daptomycin. Two patients underwent surgical debridement. Outcomes were generally favorable, with 5 patients demonstrating resolution of infection. One patient, however, died; and another patient has chronic osteomyelitis, which has required ongoing antimicrobial therapy.

DISCUSSION

This study describes the clinical features of hematogenous CNS VO in patients without prior spinal surgery. In our series, fever, rigors, or sweats were uncommon, possibly reflecting the low virulence of CNS. As has been true for VO caused by organisms other than CNS, all patients had back pain, elevation of ESR and CRP, and abnormal MRI of the spine. Most significantly, an indwelling intravascular device was present in all patients including central venous catheters in several patients receiving hemodialysis. Furthermore, all patients in whom blood cultures were performed also had CNS bacteremia. Because no patient had prior surgery or a local infection at a contiguous site, we postulate that the most likely pathogenesis of VO was hematogenous dissemination of CNS introduced via an indwelling intravascular access device with deposition of the CNS at the involved vertebral endplate followed by local involvement of the contiguous disc and vertebral body.

Previous case reports have described patients undergoing hemodialysis through shunts or fistulas as developing CNS VO. *S. epidermidis*, for example, was reported to cause hematogenous osteomyelitis in one series of 3 patients receiving hemodialysis through shunts. In another series, *S. epidermidis* was reported to cause VO in 2 patients receiving hemodialysis via shunts (Table 1).

Finally, in another report, 1 of 9 patients undergoing hemodialysis who became bacteremic with CNS developed vertebral osteomyelitis presumably through hematogenous spread. The finding of a hemodialysis catheter in each of these patients is consistent with our hypothesis that the portal of entry for the CNS bacteremia in cases of VO is likely an indwelling vascular access line, hemodialysis shunt, or other device. We were, however, able to find one case report of a patient who developed CNS VO without an indwelling line or device (Table 1).

Prior case series, although not defining the clinical features of CNS VO, have nonetheless shown that CNS is not an uncommon cause of hematogenous VO. In one series of adults with vertebral osteomyelitis with or without associated endocarditis, *S. epidermidis* was identified as a pathogen in 3% (3/91) of the cases. In another series of hematogenous VO in adults, 20% (20/98) of the cases were due to CNS that were either sensitive to methicillin (15 cases) or resistant to this antibiotic (5 cases). Other studies have identified similar findings with CNS as the cause of hematogenous VO in 15% to 16% of the cases. In children, this organism may be a less common cause of hematogenous VO. For example, in an 18-year review of 57 cases of pediatric vertebral osteomyelitis at one institution, only one case was caused by *S. epidermidis*.

Individual case reports have discussed the management of hematogenous CNS VO. In these cases, indwelling intravascular devices were removed and appropriate antibiotics instituted with resultant clinical improvement without the need for surgical debridement. Likewise, patients in our series received prolonged intravenous therapy of 6- to 12-week duration with antibiotics as determined by sensitivity testing. Most patients had
a favorable response to therapy with clinical and radiographic improvement upon completion of treatment. Few patients in our series developed complications, perhaps owing to the low virulence of CNS. For example, a paraspinal abscess developed in only one of our patients. No epidural abscess or neurological compromise developed in any of our patients. Likewise, open surgical debridement was required in only 2 of our 7 patients, and that was performed as part of a surgical procedure performed to rectify malalignment of vertebra after the infection. The second patient required surgical exploration to rule out the presence of metastatic renal cell carcinoma at the site of infection.

When CNSs are isolated from sterile culture sites such as blood cultures in patients with clinical and radiologic features of VO, physicians must assess the potential clinical relevance of this finding. In our series, physicians managing patients with clinical and radiologic features of VO were uncertain about the diagnostic significance of CNS isolated from blood cultures. There may have been several reasons that the treating physicians were hesitant to conclude that the CNS isolated from blood cultures was indeed the pathogen causing the VO. For example, CNS isolated from blood cultures are often contaminants rather than pathogens. However, CNS is known to cause infections at sites that have prosthetic material or hardware. In a study investigating 22 cases of CNS bacteremia, 3 patients were identified with postoperative vertebral osteomyelitis at the site of spinal hardware. In the absence of spinal hardware, physicians managing patients in our series were not confident that CNS, a possible contaminant of a blood culture, was indeed the cause of the VO. Consequently, physicians requested a diagnostic aspirate of the disc/vertebra to identify the causative organism.

Our study suggests that in patients with VO, indwelling vascular access devices, and other medical comorbidities, CNS isolated from multiple blood cultures should not be discounted as a contaminant even in the absence of spinal hardware. Furthermore, in CNS bacteremic patients who have an indwelling intravascular access line or device, it may not be necessary to perform an aspirate of the spine to establish the microbiologic diagnosis of VO, as the literature suggests that CNS is not an uncommon cause of hematogenous VO in patients without spinal hardware.

In conclusion, when CNS is isolated from multiple blood cultures in patients with an indwelling intravascular access line or device and clinical, laboratory, and imaging findings are consistent with VO, physicians should consider this organism to be the potential etiologic pathogen even when there is no history of spinal surgery.

REFERENCES