Hematogenous Vertebral Osteomyelitis Due to Staphylococcus aureus in the Adult: Clinical Features and Therapeutic Outcomes

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Objective: Staphylococcus aureus is the most common cause of hematogenous vertebral osteomyelitis in adults. To better define clinical features and therapeutic outcomes, the charts of 40 adult patients with S. aureus hematogenous vertebral osteomyelitis were retrospectively reviewed.

Methods: Retrospective chart review using standardized data collection form.

Results: S. aureus hematogenous vertebral osteomyelitis commonly occurred in the settings of recent invasive procedures (55% of patients), insulin use (28%), and hemodialysis (20%). Ten percent of patients had S. aureus bacteraemia or vascular catheter infection within the preceding 6 months. Median time from first symptom to diagnosis was 51.3 days. A portal of entry for S. aureus was identified in 13 patients (32.5%); intravenous catheters were the likely origin in 9 of those 13 patients. Concurrent endocarditis was present in 4 patients. Forty-eight percent of patients had neurologic abnormalities and 60% of patients had an epidural, paraspinal, or psoas abscess demonstrated by neuroimaging. S. aureus was isolated through fine-needle aspiration in 17 of 23 patients (74%) and from blood cultures in 23 of 34 patients (68%). Infection was due to methicillin-susceptible S. aureus in 67.5% of patients. All patients received intravenous antibiotics for a mean duration of 58.6 days; 36 of 40 (90%) also received concomitant rifampin. Twenty-seven percent and 12.5% of patients underwent surgical debridement and CT-guided drainage of abscesses, respectively. After intravenous therapy, 19 of 30 eligible patients received oral continuation treatment. The mean duration of total antibiotic therapy was 142.2 days.

Conclusions: Cure of infection was achieved in 83% (24/29) of evaluable patients, but 50% of those achieving cure still had infection-related sequelae. Intravenous antibiotic therapy for at least 8 weeks was the only clinical factor associated with cure (P = 0.05, two-tailed Fisher exact test).

Key Words: osteomyelitis, spondylitis, Staphylococcus aureus, vertebral osteomyelitis

Staphylococcus aureus (SA) is the most common cause of hematogenous vertebral osteomyelitis (HVO) in the adult,1–3 accounting for 40 to 45% of all cases.3–11 Recent observations suggest that the incidence of SA HVO is increasing,12–14 yet risk factors for acquisition of SA HVO and the cause for this increase in incidence are largely unknown. Contributing factors may include the aging of the population,15 the more frequent performance of invasive medical procedures, and the increasing use of indwelling intravascular devices, often for long durations. The latter two factors may predispose patients to local and bacteremic SA infections, the necessary first steps in the pathogenesis of HVO. Management of SA HVO varies considerably from institution to in-

Key Points
- Vertebral osteomyelitis should be a diagnostic consideration in any patient with back pain and Staphylococcus aureus bacteremia.
- Vascular catheters are a frequent portal of entry for S. aureus to gain access to the bloodstream before vertebral seeding.
- Neurologic findings are often present at the time of diagnosis and serve to identify patients who may have complicating abscesses that require drainage.
- Methicillin-resistant S. aureus is the causative organism in approximately one third of patients.
- A minimum parenteral treatment duration of 8 weeks is usually warranted.
stitution, with the duration of recommended parenteral antimicrobial therapy often ranging from 4 to 8 weeks. Other aspects of management are also poorly defined. The potential benefit of oral continuation therapy after the completion of parenteral antibiotic treatment and the role, if any, for synergistic therapy with rifampin have not been well studied. In addition, indications for percutaneous drainage of abscesses and for surgical intervention in patients with SA HVO have not been standardized. Last, only Jensen et al have commented on outcome in patients with SA HVO. Therefore, the goals of this study were to better define the clinical features and therapeutic outcomes in patients with SA HVO.

Materials and Methods

The Wake Forest University Baptist Medical Center is an approximately 800-bed tertiary care hospital located in Winston-Salem, NC. The population served by the Medical Center is a mixture of primary care and referral patients, with emphasis on cardiology, oncology, and nephrology.

The medical records of patients 18 years of age or older who were hospitalized at Wake Forest University Baptist Medical Center between 1994 and 2000 with a discharge diagnosis of vertebral osteomyelitis (VO) were retrospectively reviewed. To be included in the study, patients had to manifest a clinical illness compatible with spinal infection, exhibit radiographic evidence of VO by any imaging modality, and demonstrate a positive culture for SA from the site of infection (bone, disc space, associated abscess) or from blood. Patients with prior back surgery or a history of penetrating trauma at the site of documented osteomyelitis in the previous 6 months were excluded from the study. Forty unique patients were identified.

The initial day of hospitalization was considered to be the first day the patient was admitted to any hospital with signs and symptoms subsequently attributed to SA HVO. Fever was considered to be present if the patient had a temperature of 38° or greater that occurred before, or within 1 week after, the diagnosis of VO was established. A potential portal of entry was thought to exist if the patient had a culture-documented extravertebral focus of infection with SA with an antibiogram identical with that of the organism subsequently isolated from bone, abscess, or blood and that predated the development of signs and symptoms suggestive of VO. Radiographic studies were all interpreted by staff radiologists, and conventional published criteria were used to make a radiographic diagnosis of VO. Microbiologic confirmation of the diagnosis of SA HVO was considered to have occurred if SA was isolated from one or more blood cultures or from a culture obtained from involved bone, disc space, or paravertebral or epidural abscesses.

Once the diagnosis of SA HVO was established, all treatment decisions were made by the primary care team and/or the involved consultants. The antimicrobial regimen chosen, the duration of parenteral therapy, and the decision to use oral continuation therapy after a course of parenteral treatment was completed were at the discretion of the managing team and were not dictated by a predetermined protocol or study. For the purposes of this retrospective study, patients were deemed to be eligible for oral continuation therapy if they had completed at least 4 weeks of parenteral treatment (a minimum conventional duration of therapy). If patients died or were lost to follow-up before completing 4 weeks of parenteral therapy, they were classified as ineligible for oral continuation therapy. The decision to order and the timing of follow-up laboratory and radiographic studies were per the primary care team or managing physician.

Outcomes of infection were classified according to predetermined categories. Cure of infection was considered to have been achieved if patients exhibited no symptoms or signs of active infection by clinical, laboratory, and/or radiographic evaluation at the end of therapy (both intravenous and oral administration) and for a minimum of 6 months thereafter. Patients who were judged to be cured of infection were then subclassified as having cure without sequelae or cure with sequelae. Sequelae of infection were considered to be those findings occurring as a consequence of infection that persisted for at least 3 months after completion of therapy. Unresolved pain (local or radicular), voiding dysfunction, extremity weakness, and hyporeflexia were the specific sequelae that were identified. Patients who died while receiving therapy for HVO were classified as having death caused by infection or death caused by their underlying diseases and/or other causes. Death caused by infection was judged to have occurred if a patient died within 14 days of initiation of appropriate therapy (eg, treatment with a specific antistaphylococcal antimicrobial agent such as nafcillin, cefazolin, or vancomycin to which the patient's isolate was susceptible) or in conjunction with breakthrough SA bacteremia while receiving ongoing therapy. Relapse of infection was defined as recurrent back pain and fever in conjunction with an increasing erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) with or without worsening radiographic findings occurring after the completion of therapy. Relapse of infection was microbiologically confirmed if recurrent bacteremia or new positive cultures from the previously infected site were documented. Patients were judged to be unevaluable as to outcome if they were lost to follow-up while still receiving ongoing antibiotic therapy.

The two-tailed Fisher exact test and the Student t test were used for statistical analysis. A P value of 0.05 or less was considered significant.

Results

Patient demographics

Forty patients were identified as having SA HVO. The mean age for study patients was 62 years. Thirty-five patients
(87.5%) were over the age of 50 and 16 patients (40%) were over the age of 65. Twenty-four of 40 (60%) were male. Thirty-one (77.5%) were white and 9 (22.5%) were black. Six of 40 patients (15%) had been hospitalized in the 2 weeks preceding admission; 8 of 40 (20%) had received antimicrobial therapy of some type in that same period. Three of 40 (7.5%) had been residents in chronic care facilities during the 2 weeks before admission.

**Comorbid diseases and preceding procedures**

Most patients with SA HVO had chronic underlying medical diseases (Table 1). Of note, 28% had insulin-dependent diabetes mellitus and 20% were undergoing hemodialysis for end-stage renal disease (ESRD). A history of back injury within the preceding 6 months was elicited from 7 of 40 patients (17.5%). Only 3 of 40 patients were injection drug users. Invasive procedures had been performed in 22 patients (55%) in the previous 6 months. The most common of those procedures included placement of vascular lines (13 patients, 35%), open surgical procedures (10 patients, 25%), bladder catheterization (9 patients, 23%), and mechanical ventilation (2 patients, 5%). Four patients (10%) had a documented SA bacteremia or SA vascular catheter infection in the 6 months preceding their diagnosis of VO.

**Clinical features**

The mean duration of symptoms before hospital admission was 47.6 days (range, 1 to 365 days) and the average time from first symptom to diagnosis of SA HVO was 51.3 days (range, 1 to 365 days). The most common symptoms and signs on hospital admission are shown in Figure 1. Fever was present in only 35% of patients. Nineteen of 40 (48%) patients had a neurologic abnormality on initial examination (Fig. 1). Based on clinical and microbiologic evaluation, a potential portal of entry for the hematogenous dissemination of SA was identified in 13 patients (32.5%). Intravenous catheters were the likely origin in 9 of those 13 patients. The remaining 4 patients with documented portals of entry had pleural empyema, an infected pseudocyst, an infected knee prosthesis, and an infected AV fistula as the sources for their bacteremias. The average length of hospital stay during the admission when the diagnosis of SA HVO was established was 40.1 days (range, 5 to 170 days).

**Laboratory findings**

Thirty-two of 40 patients (80%) had leukocytosis at admission. The average admission white blood cell count for all patients was 16, 200/mm³. The ESR was elevated in 35 of 36 (97.2%) patients; the mean peak ESR for all 36 patients was 101 mm/hr (range, 13 to >140). Of the 17 patients who had CRP levels performed, 15 (88.2%) had values above normal with the average maximum CRP being 10.9 mg/dL (range, 1.7 to 31.4).

**Radiographic evaluation**

All patients had diagnostic radiographic studies performed (Table 2). MRI was the most frequently ordered radiographic test, with 35 of 36 studies (97%) demonstrating abnormalities consistent with VO (Fig. 2). The radiographic localization of disease is shown in Figure 3. The thoracic spine was the site of infection in 52.5% of patients.

**Contiguous and metastatic foci**

Contiguous abscesses associated with foci of VO were present in 24 of 40 patients (60%). Of those 24 patients, 16 had epidural abscesses, 8 had paraspinal abscesses, 4 had psoas abscesses, and 2 had pleural empyemases. Other concurrent foci of active SA infection included endocarditis (4/40 patients, 10%), septic arthritis (2/40 patients, 5%), septic pulmonary emboli (1 patient, 2.5%), and an infected pancreatic pseudocyst (1 patient, 2.5%). No patient had concurrent meningitis.

**Microbiology**

According to study definition, all patients had a positive culture for SA from blood, from spine (vertebral body or disk), or from an abscess contiguous to the spine. SA was isolated by CT-directed fine-needle aspiration (FNA) of bone, disk space, or abscess in 17 of 23 patients (74%). Blood cultures grew SA in 23 of 34 patients (68%). Both blood cultures and local cultures were positive in 12 of 40 patients (30%), whereas 14 patients (35%) had positive blood cultures.

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**Table 1. Underlying medical conditions**

<table>
<thead>
<tr>
<th>Underlying disease</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>14/40</td>
<td>35.0</td>
</tr>
<tr>
<td>Insulin-dependent</td>
<td>11/14</td>
<td>27.5</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>9/40</td>
<td>22.5</td>
</tr>
<tr>
<td>ESRD with hemodialysis</td>
<td>8/40</td>
<td>20.0</td>
</tr>
<tr>
<td>History of back injury</td>
<td>7/40</td>
<td>17.5</td>
</tr>
<tr>
<td>Immunosuppressive therapy in previous 4 weeks</td>
<td>6/40</td>
<td>15.0</td>
</tr>
<tr>
<td>COPD</td>
<td>6/40</td>
<td>15.0</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>4/40</td>
<td>10.0</td>
</tr>
<tr>
<td>Malignancy</td>
<td>4/40</td>
<td>10.0</td>
</tr>
<tr>
<td>Rheumatologic conditions</td>
<td>4/40</td>
<td>10.0</td>
</tr>
<tr>
<td>Remote history of back surgery</td>
<td>3/40</td>
<td>7.5</td>
</tr>
<tr>
<td>IVDU</td>
<td>3/40</td>
<td>7.5</td>
</tr>
<tr>
<td>HIV infection</td>
<td>2/40</td>
<td>5.0</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>1/40</td>
<td>2.5</td>
</tr>
<tr>
<td>Venous stasis ulcers</td>
<td>1/40</td>
<td>2.5</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1/40</td>
<td>2.5</td>
</tr>
</tbody>
</table>

*ESRD, end-stage renal disease; COPD, chronic obstructive pulmonary disease; IVDU, intravenous drug use. HIV, human immunodeficiency virus.*
only and 14 patients (35%) had positive local cultures only. Overall, 27 of 40 patients (67.5%) had methicillin-susceptible SA (MSSA), 12 of 40 (30%) had methicillin-resistant SA (MRSA), and 1 of 40 (2.5%) had both. All SA isolates were susceptible to rifampin by in vitro testing.

**Treatment**

All patients received parenteral antibiotics as a component of their initial treatment. Concomitant rifampin (intravenous or oral administration) was administered in conjunction with intravenous antibiotics in 36 of 40 patients (90%). The average duration of intravenous antibiotic therapy was 58.6 days, with 23 of 40 patients (57.5%) receiving 8 weeks or more of parenteral treatment. Nineteen of 30 patients (63%) who completed a course of parenteral treatment received oral continuation therapy. The average duration of oral continuation therapy was 27.4 weeks (range, 2 to 196 weeks). Total antibiotic therapy (both parenteral induction and oral continuation) was administered for an average duration of 142.2 days. The key features of antibiotic treatment are summarized in Table 3.

In addition to antimicrobial therapy, 16 patients (40%) also underwent surgical debridement (n = 11) or CT-guided drainage procedures (n = 5). Surgery was performed most often in patients with neurologic signs/symptoms at admission (9 of 19 patients [47%] with neurologic signs/symptoms underwent surgery versus 2 of 21 patients [10%] without neurologic abnormalities) and in patients with radiographically documented epidural, paraspinal, or psoas abscesses (10 of 24 patients [41.7%] with abscesses underwent surgery versus 1 of 16 patients [6.3%] without an abscess). CT-guided percutaneous catheter drainage of abscesses was performed in

**Table 2. Radiographic studies**

<table>
<thead>
<tr>
<th>Type</th>
<th>No. of patients studied (% of total)</th>
<th>No. abnormal (% of total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain films of spine</td>
<td>21 (52.5%)</td>
<td>17 (80.9%)</td>
</tr>
<tr>
<td>Bone scan</td>
<td>13 (32.5%)</td>
<td>10 (76.9%)</td>
</tr>
<tr>
<td>Gallium scan</td>
<td>2 (5%)</td>
<td>2 (100%)</td>
</tr>
<tr>
<td>CT of spine</td>
<td>14 (35%)</td>
<td>13 (92.8%)</td>
</tr>
<tr>
<td>MRI of spine</td>
<td>36 (90%)</td>
<td>35 (97.2%)</td>
</tr>
</tbody>
</table>

*Refer to References 2 and 17 to 21 for definitions of abnormal findings.

**Fig. 1** Signs and symptoms on admission. DTR, Deep tendon reflex.

**Fig. 2** A, T1-weighted MRI image of the spine shows collapse of the T11 and T12 vertebral bodies with focal kyphosis in a patient with methicillin-susceptible Staphylococcus aureus diskitis and osteomyelitis. B, T1-weighted MRI image with gadolinium enhancement shows osseous destruction of T11-T12 with surrounding soft tissue enhancement in a patient with methicillin-susceptible S aureus diskitis and osteomyelitis.
5 patients (12.5% of total). Of the 5 patients who underwent CT-guided drainage, none had neurologic signs and symptoms at admission.

**Therapeutic outcomes**

Of the 40 patients with SA HVO, 7 died before completing antimicrobial therapy for their infection. Three of these deaths were due to uncontrolled SA infection (2 of those 3 had received less than 4 weeks of parenteral therapy for their infection), whereas the other 4 deaths were secondary to progression of underlying diseases (all had received more than 4 weeks of parenteral therapy). Of note, 6 of the 7 patients who died as a result of any cause and all 3 of the patients with infection-related deaths had infection caused by MRSA. Thus, the all-cause mortality rate was 17.5%, with an infection-related mortality rate of 7.5%. Among the 33 remaining patients, 4 were lost to follow-up, with their ultimate outcomes unknown. Of those 4 patients, 3 were still receiving parenteral therapy and 1 was receiving oral therapy. None of those patients had persistent symptoms or signs of active infection when last evaluated. Twenty-nine patients survived their infection and were evaluable for outcome. Twenty-four of those 29 patients (83%) were judged to have been cured of their infection, whereas 5 patients (17%) had relapse of their infection. Among the 5 patients with relapsing infection, relapse was clinically documented in 1 patient and clinically plus microbiologically documented in 4 patients. Of the 24 patients who were cured of infection, 12 (50%) had infection-related sequelae: 7 of 12 (58%) with persistent local or radicular pain, 5 of 12 (42%) with lower extremity weakness, 3 of 12 (25%) with voiding dysfunction, and 3 of 12 (25%) with lower extremity hyporeflexia. In addition, among the patients who had relapsing disease, 1 had persistent local pain, 1 had lower extremity weakness, and 2 had voiding dysfunction. Thus, sequelae of infection were present in 15 of 29 (52%) surviving, evaluable patients, with 8 of those 29 patients (28%) manifesting neurologic sequelae.

Comparative clinical characteristics of the patients who were cured of their infection versus those who had relapse of infection are summarized in Table 4.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cure (n = 24)</th>
<th>Relapse (n = 5)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSSA</td>
<td>20 (83%)</td>
<td>3 (60%)</td>
<td>0.55</td>
</tr>
<tr>
<td>≥8 weeks intravenous Rx</td>
<td>17 (71%)</td>
<td>1 (20%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Oral continuation Rx</td>
<td>16 (67%)</td>
<td>2 (40%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>22 (92%)</td>
<td>3 (60%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7 (29%)</td>
<td>2 (40%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>3 (13%)</td>
<td>0 (0%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Drainage</td>
<td>12 (50%)</td>
<td>0 (0%)</td>
<td>0.06</td>
</tr>
<tr>
<td>≥60 days of symptoms at diagnosis</td>
<td>8 (33%)</td>
<td>2 (40%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*MSSA, Methicillin-susceptible Staphylococcus aureus, Rx, medication.*

*As determined by two-tailed Fisher exact test.

*Surgical or CT-directed percutaneous drainage.*
infection are shown in Table 4. As shown, receipt of at least 8 weeks of parenteral antibiotic therapy predicted cure of infection. No other clinical variable correlated with cure, although drainage of abscesses, either percutaneously or surgically, also seemed to improve outcome. Of note, patients with infection caused by MSSA were not more likely statistically to achieve cure than were patients with MRSA HVO.

**MSSA versus MRSA**

A comparison of clinical features, treatment, and outcomes in patients with infection caused by MSSA versus those with MRSA is shown in Table 5. Patients with MRSA were no more likely than patients with MSSA to have neurologic abnormalities at admission, contiguous abscesses, or metastatic foci of infection. Concurrent use of rifampin and drainage of abscesses did not differ between the two groups. The likelihoods of cure of infection and survival without sequelae were also not influenced by the causative organism's susceptibility to methicillin. However, both all-cause death and infection-related death were statistically more likely to occur in MRSA-infected than in MSSA-infected patients.

**Discussion**

*Staphylococcus aureus* is the most common cause of HVO. According to our data and those of Jensen et al.,

**TABLE 5. Comparison of patients with MSSA versus MRSA hematogenous vertebral osteomyelitis**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MSSA (%)</th>
<th>MRSA (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes (n = 39)†</td>
<td>9/27 (33)</td>
<td>4/12 (33)</td>
<td>1.0</td>
</tr>
<tr>
<td>ESRD (n = 39)</td>
<td>4/27 (15)</td>
<td>4/12 (33)</td>
<td>0.22</td>
</tr>
<tr>
<td>Duration of symptoms at diagnosis (n = 37)</td>
<td>59.3 d</td>
<td>39.4 d</td>
<td>0.2</td>
</tr>
<tr>
<td>Neurologic findings at diagnosis (n = 39)</td>
<td>14/27 (52)</td>
<td>5/12 (42)</td>
<td>0.73</td>
</tr>
<tr>
<td>Contiguous abscesses (n = 39)</td>
<td>17/27 (63)</td>
<td>7/12 (58)</td>
<td>1.0</td>
</tr>
<tr>
<td>Metastatic foci (n = 39)</td>
<td>5/27 (19)</td>
<td>3/12 (25)</td>
<td>0.68</td>
</tr>
<tr>
<td>Drainage of abscess(es) (n = 39)</td>
<td>11/27 (41)</td>
<td>4/12 (33)</td>
<td>0.73</td>
</tr>
<tr>
<td>Rifampin (n = 39)</td>
<td>23/27 (85)</td>
<td>12/12 (100)</td>
<td>0.29</td>
</tr>
<tr>
<td>Cure of infection (n = 28)</td>
<td>20/23 (87)</td>
<td>4/5 (80)</td>
<td>1.0</td>
</tr>
<tr>
<td>Survival without sequelae (n = 28)</td>
<td>11/23 (48)</td>
<td>4/5 (80)</td>
<td>0.33</td>
</tr>
<tr>
<td>All-cause mortality (n = 35)</td>
<td>1/24 (4)</td>
<td>6/11 (55)</td>
<td>0.002</td>
</tr>
<tr>
<td>Infection-related mortality (n = 35)</td>
<td>0/24 (0)</td>
<td>3/11 (27)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*S. aureus, methicillin-resistant S. aureus; ESRD, end-stage renal disease.*

†Comparison of proportions assessed by Student t-test. Comparison of means performed by Student t-test.

‡Number of evaluable patients for the parameter under consideration. The patient with infection caused by both MSSA and MRSA was excluded from all comparisons. Mortality was assessable for all patients except one patient with combined infection and four patients who were lost to followup. See Materials and Methods section for definitions of cure of infection, sequelae of infection, and death caused by infection.

Typical patients who acquire this infection are older males with one or more comorbid conditions that may be associated with immunologic dysfunction and patients with chronic diseases that require permanently implanted indwelling vascular access devices for their treatment. Patients with diabetes mellitus comprised one third of our study population with SA HVO. As several other studies have noted, diabetics appear to be at increased risk for HVO, although specific predisposing factors have not been clearly identified. Notably, 20% of patients in this series had ESRD, a greater proportion with that underlying diagnosis than has been reported previously in other studies of HVO. The chronically implanted vascular access devices that patients with ESRD require place them at increased risk for Gram-positive coecal bacteremias and associated deep-seated metastatic infections. Recently, Steinberg et al. observed that 56% of nosocomial SA bacteremias and 22% of community-acquired SA bacteremias occurring between 1990 and 1993 were associated with vascular devices. Sixty-nine percent of the patients in our series with an identifiable portal of entry were found to have an intravenous catheter as a source. This observation suggests that vascular access devices are an important risk factor for SA HVO. Few other studies have specifically focused on SA in their analysis of patients with HVO and hence intravenous catheters have been less commonly identified as a source for vertebral seeding. Jensen et al. also studied SA HVO but noted the skin to be the most common source for SA in their patients with HVO; however, less than 1% of their patients had chronic renal failure as a comorbid condition.

Of particular note is our observation that 10% of patients with SA HVO had a preceding SA bacteremia or vascular catheter infection within the preceding 6 months. Other authors have emphasized the potential late sequelae such as osteomyelitis that may occur as a consequence of incompletely or inadequately treated SA bacteremias. It is thus conceivable that suboptimal treatment of their original infections may have predisposed those four patients to the subsequent development of vertebral osteomyelitis. The message is clear: SA bacteremias have a significant risk for morbidity and must be treated aggressively. As a corollary, any patient with a recent history of SA bacteremia who then has development of persistent or severe back pain must be considered to have VO until proven otherwise and should undergo appropriate diagnostic imaging.

The presenting signs and symptoms of SA HVO are often vague, but most patients with VO (92.5% in our series) have localized back pain. Only one third of our patients had fever, a lower percentage than has been reported previously. Approximately one half of our patients had some type of neurologic finding on presentation. This observation is particularly important because those patients with neurologic abnormalities are more likely to have an epidural abscess or spinal instability that may require immediate surgical intervention.

In our series, 47% of patients with
neurologic abnormalities at admission required surgical intervention compared with 10% of those without neurologic abnormalities. Likewise, 41.7% of patients with an associated abscess (ie, epidural, paraspinal, psoas) required surgical intervention as opposed to 6.3% without an associated abscess. Rapid diagnosis and intervention appear to be needed in this subset of patients if long-term sequelae such as paralysis are to be prevented.

As the literature attests, and as our study affirms, radiographic imaging of the spine is critical in providing support for a diagnosis of VOD and in identifying complicating features of vertebral infection. MRI proved to be the most sensitive radiographic study in our patient population and is generally viewed as the radiographic modality of choice for VOD. CT scans are also highly sensitive in detecting abnormalities of bone and disk space but are perhaps less sensitive in detecting complicating features. If MRI or CT scans are not readily available and plain films are nondiagnostic, gallium scanning should be considered as an alternative diagnostic study, especially if paired with technetium bone scans, since available literature suggests that sensitivity may approach 90%. In contrast, indium scans have proven to be somewhat insensitive in detecting vertebral infection and should not be used in the evaluation of patients with possible VOD.

The diagnosis of SA HVO can be confirmed microbiologically in most patients. Blood cultures were positive in 68% of our patients, a rate higher than that observed by Jensen et al but comparable to that reported in other studies of VOD. Since a single organism causes the vast majority of cases of HVO, blood cultures should always be a part of the initial diagnostic evaluation of patients with suspected HVO because those cultures will frequently yield the causative pathogen. However, the use of blood cultures should not preclude attempts at obtaining cultures directly from involved bone or paraspinous tissues. In our study, the diagnostic yield of cultures obtained through FNA was high, with 74% of those procedures producing positive cultures for SA. In contrast, Jensen et al reported that FNA and open biopsy yielded positive cultures in only 40% of their patients. They speculated that the relatively low yield of those procedures may have been due to the preferential use of FNA rather than cutting needles for specimens and the frequent administration of antibiotics before the procedure. It could be argued that if patients have a compatible clinical syndrome, an abnormal MRI consistent with VOD, and a positive blood culture for SA, that the diagnosis of SA HVO has been established and that FNA or open biopsy is thus not warranted. Although preliminary data would support that observation, direct sampling of the involved vertebral body or disk space is still probably preferable in most cases to provide direct microbiologic confirmation of the diagnosis. Certainly in those cases when blood cultures are negative, FNA for culture should be pursued. If the FNA is also negative, conventional wisdom would then dictate that an open surgical biopsy be obtained.

On the basis of this retrospective study and our literature review, several observations about therapy can be offered. First, the optimal duration of antimicrobial therapy in SA HVO has not been well established. The standard reference text for infectious diseases suggests a treatment duration of 4 to 6 weeks for patients with VO. Osenbach et al recommended 6 to 8 weeks of parenteral therapy and expressed the belief that additional oral therapy is generally not required. Other authors believe that 4 weeks of therapy is adequate and that relapse of infection after 4 weeks is an indication for surgical intervention. Still others have recommended 4 to 6 weeks of parenteral treatment with a change to oral continuation therapy if clinical and laboratory markers have improved but have not normalized by the end of the parenteral course. More recently, Jensen et al have suggested that a minimum of 8 weeks of treatment is needed to achieve optimal cure rates, particularly for SA HVO. Patients in our series had better outcomes when they were treated with at least 8 weeks of intravenous antibiotic therapy. Those receiving less than 8 weeks of parenteral therapy were less likely to be cured. Thus, on the basis of our experience and that of Jensen et al, we would recommend a minimum 8-week course of parenteral antibiotic therapy for patients with SA HVO to optimize outcomes. Second, rifampin is often used for synergistic therapy in the treatment of serious, deep-seated, or protected SA infections such as HVO. Excellent penetration into most tissues, including cancellous bone, and into phagocytic vacuoles within neutrophils and tissue macrophages, a reported protected sanctuary for SA, makes rifampin an attractive option for use in HVO. In animal models of chronic osteomyelitis, rifampin in combination with any other active agent has been shown to be much more effective than any single active therapy in achieving cure of infection. In our series, rifampin was used as adjunctive synergistic therapy in most patients (90%). Hence, a statistically significant improvement in patient outcome could not be demonstrated for those patients who received rifampin. Nevertheless, we believe that experience with rifampin in animal models of osteomyelitis and in other complicated SA bone and joint infections argue for its use. Third, the use of oral continuation therapy might be beneficial in selected patients. In particular, if a patient with SA HVO has received 8 weeks of parenteral therapy and the ESR and/or CRP still have not normalized, then the use of oral continuation therapy should be considered, a recommendation also advocated by McHenry et al. However, even if elected, the optimal duration of oral continuation therapy remains unknown.

Unlike the Jensen study that was conducted in Denmark, where MRSA is uncommon, approximately 30% of the patients in this series were infected with MRSA. Of the 12 patients in our study with MRSA as a cause of SA HVO, 11 had a risk factor for MRSA infection. Six patients had...
vascular access catheters and spent considerable time in the hospital or at a hemodialysis center before the diagnosis of SA HVO. Two patients were nursing home residents and three other patients had been hospitalized in the previous 6 months. Therefore, clinicians should be attuned to the possibility of MRSA as a cause for SA HVO in patients who have recently been in hospitals, nursing homes, or hemodialysis centers. In patients with risk factors for MRSA, empiric treatment with vancomycin while awaiting susceptibility studies would certainly be justified.

The impact of methicillin resistance on the outcome of serious SA infections still remains somewhat controversial,42–45 Among our study patients who were eligible for cure of their infection, the presence of MRSA as the causative organism was not correlated with a greater risk for treatment failure and relapse (Table 4). However, patients with MRSA were significantly more likely to die, both from all causes and as a direct consequence of their infection (Table 5). That finding is in keeping with a recently published meta-analysis of 31 studies of SA bacteremia by Cosgrove et al46 that revealed that infection with MRSA doubled the risk of death. Similarly, Kim et al47 found that among patients with non-eradicable foci of SA infection (such as vertebral osteomyelitis) and complicating bacteremia, a significantly greater proportion with MRSA infection died. Thus, deep-seated foci of SA infection such as vertebral osteomyelitis may confer an increased risk of infection-related death if MRSA is the causative organism.

Conclusion

SA HVO can be a devastating medical illness with significant morbidity and mortality rates, especially in elderly patients. Since recent observations suggest that the incidence of SA HVO is increasing,13 the diagnosis should be entertained in any patient with back pain, fever, neurologic abnormalities, underlying diabetes or ESRD, or a history of recent instrumentation (especially vascular access). Patients with risk factors for this infection, compatible signs and symptoms of VO, SA bacteremia of unknown source, and possibly unexplained fevers should be considered for diagnostic evaluation. The imaging modality of choice is MRI. Patients with neurologic abnormalities on examination, spinal instability, and/or associated abscesses are more likely to require surgical intervention, and prompt consultation with a neurosurgeon is recommended. Antimicrobial therapy should be directed toward the organism identified by blood culture, FNA, or open biopsy. Those patients who have risk factors for MRSA infection should be treated empirically with vancomycin until culture results are known. Among factors potentially influencing outcome, the administration of at least 8 weeks of parenteral therapy has the greatest impact on cure. Patients with infection caused by MRSA appear to have a higher risk of dying than do patients with MSSA.

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References

Priest and Peacock • S aureus Vertebral Osteomyelitis

36. Norden CW. Experimental chronic staphylococcal osteomyelitis in rab-


Please see Michael S. Gelfand and Kerry O. Cleveland's editorial on page 853 of this issue.

Nature magically suits a man to his fortunes, by making them the fruit of his character.

—Ralph Waldo Emerson