Bacteremic *Staphylococcus aureus* Spondylitis

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**Background:** The incidence of hematogenous *Staphylococcus aureus* osteomyelitis of the vertebral column is rapidly increasing and few studies dealing with the diagnosis, treatment, and outcome of this severe disease are available.

**Methods:** Based on a nationwide registration, the clinical and bacteriological data were reviewed from 133 cases with a positive blood culture for *S aureus* and symptoms of vertebral osteomyelitis in Denmark for the period 1980 to 1990.

**Results:** The 133 cases of vertebral *S aureus* osteomyelitis reviewed were mainly community-acquired infections (82%) in older patients (median age, 65 years) and often occurred with underlying diseases. Both symptoms and laboratory values were relatively unspecific. Bone scan methods proved to be more optimal for diagnosis of vertebral *S aureus* osteomyelitis in the early stages compared with conventional radiography that proved a lack of consistency in the formative stages. The infection was mostly (70%) localized in the lower part of the column. The recurrence rate and rate of therapeutic failure depended on the duration and dosage of penicillinase-stable penicillins, respectively. Patients treated with fusidic acid in addition to penicillinase-stable penicillins had a significantly lower recurrence rate. Based on these findings, we recommend treatment with penicillinase-stable penicillins and fusidic acid for a total of 8 weeks, with a daily dosage of penicillinase-stable penicillins higher than 4 g.

**Conclusions:** The diagnosis of vertebral *S aureus* osteomyelitis based on clinical findings is difficult to ascertain. Bone scans are necessary because radiographic methods do not detect disease as early. Treatment with penicillinase-stable penicillins, at least 4 g/d for at least 8 weeks, is recommended.

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**RESULTS**

**BACTERIA AND ANTIBIOTIC RESISTANCE**

The pattern of bacteriophage types and antibiotic resistance of bacteremic *S aureus* strains isolated from patients with vertebral osteomyelitis compared with other strains isolated from blood in Denmark during the same period is shown in *Table 1*. Strains of bacteriophage group I and II were more prevalent among vertebral osteomyelitis cases, and the strains from vertebral osteomyelitis were more commonly susceptible to penicillin (Table 1).

**SOURCE OF INFECTION**

Of the 133 patients with hematogenous vertebral osteomyelitis, 109 (82%) had community-acquired infection and 24 (18%) had hospital-acquired infection. The majority of patients (75/109 [69%]) with community-acquired infections were admitted to departments of internal medi-
MATERIALS AND METHODS

SELECTION OF CASES

Since 1960, almost all S aureus isolates from blood cultures in Denmark have been referred for bacteriophage typing at the Staphylococcus Laboratory, Statens Serum Institut, Copenhagen. Additionally, hospital departments from all over the country have contributed data from those patients. From 1980 through 1990, a total of 8739 cases of S aureus bacteremia were registered, and 309 of these cases had underlying hematogenous osteomyelitis. Of these, 145 cases had vertebral osteomyelitis. For the present study, hospital departments were asked to submit all medical records for these patients, and a total of 133 medical records (92%) were received, which constituted the study material.

BACTERIOPHAGE TYPING AND ANTIBACTERIAL SENSITIVITY TESTING

All S aureus strain isolates were classified into bacteriophage types according to the method of Blair and Williams using the current international criteria for typing bacteriophages. The bacteriophages were used in concentrations of routine dilution (RTD): 100×RTD and 1000×RTD. The subdivision into bacteriophage groups and complexes was achieved according to criteria established by Parker. Susceptibility to antibiotics of the infecting strains was determined using a disk diffusion method. The testing was composed of susceptibility to penicillin, streptomycin, tetracycline, erythromycin, methicillin, and gentamicin.

CLINICAL DATA AND DEFINITIONS

Hematogenous osteomyelitis was defined as cases in which the bacteria had reached the bone via the circulation. For all cases the localization of vertebral osteomyelitis was determined using the results of conventional radiography, bone scintigraphy, and computed tomographic (CT) scanning. From review of the medical records the following data were extracted: age and sex of the patient; any underlying diseases and/or conditions, including cytostatic and immunosuppressive therapy, drug addiction, and recent surgery (Table 2); duration from onset to admission in community-acquired cases, duration from onset to the establishment of diagnosis, and duration from onset to start of treatment. Previous back surgery included any operation of the back in the anamnesis of the patient unrelated to the present infection.

The following parameters were extracted from the results of conventional radiography: soft tissue swelling, narrowed intervertebral disk space, degenerative changes, bone sclerosis, and bone fusion. Two or more findings were considered radiographically evident for osteomyelitis. Results of a CT scan were considered abnormal when bone and/or disk destruction was demonstrated, and results of bone scintigraphy were abnormal when the scan showed an increased uptake of tracer in the affected area. Sleep disturbance and anorexia were defined as any feelings of decreased ability to sleep and eat, respectively, compared with the patient’s habitual conditions. Back pain was determined as any pain or tenderness related to the back. Unexplainable fever was defined as an increased body temperature that could not be related to any diseases or particular determination on admission, and pyrexia was defined as a rectal temperature higher than 37.5°C. Local tenderness was defined as pain related to palpation or percussion of the spine. The following laboratory values were considered abnormal: erythrocyte sedimentation rate (ESR) greater than 15 mm/h for males and greater than 20 mm/h for females; white blood cells greater than 15.5×10⁹/L (for ages 3-12 years) or greater than 11.0×10⁹/L (for ages older than 12 years); neutrophils greater than 80%; and alkaline phosphatase greater than 800 U/L (for ages 2-10 years), higher than 1000 U/L (for ages 11-18 years), higher than 275 U/L (for ages 19-70 years), or higher than 400 U/L (for ages older than 70 years).

Complications were local spreading of the infection, such as extravertebral abscesses. Outcome parameters were recurrence, sequelae, or mortality. Recurrence was defined as a new blood culture positive for S aureus after the end of antibiotic treatment within 3 months after the first positive blood culture. Sequelae were defined as persisting signs and symptoms related to osteomyelitis lasting 3 months or longer after clinical recovery. Death was considered directly related to osteomyelitis if the patient died within 10 days after a positive blood culture or if the patient died in connection with recurrence of S aureus bacteremia. Antibiotic treatment was considered consistently registered concerning the dosage and the duration of treatment. Failure of therapy was defined as a new blood culture positive for S aureus recurring during treatment. Failure of therapy and recurrence were evaluated according to dosage and duration, respectively. Other types of treatments included immobilization procedures (corset or body cast) and surgical procedures (abscess drainage or decompressive laminectomy).

STATISTICAL METHODS

The χ² test with or without Yates correction and the Mann-Whitney U test were applied; P < .05 was considered significant. The χ² test for trend was used to test for trends in proportions as a function of dosage.
PATIENT CHARACTERISTICS

Figure 1 shows the age distribution for patients with vertebral Staphylococcus aureus osteomyelitis. Osteomyelitis of the vertebral column is mainly found among older patients, since 87 patients (65%) were aged 60 years or older. The median age was 65 years (range, 6-86 years) for all cases. Seventy (53%) were males and 63 (47%) were females. Most patients had underlying, often chronic, diseases, as shown in Table 3. Only 11 patients (8%) had no underlying diseases or conditions and 8 patients (6%) had previous back surgery not related to the current infection.

PORTAL OF ENTRY AND VERTEBRAL LOCALIZATION

The primary focus of infection is shown in Table 4. The most common focus was the skin (21%), followed by the urinary tract (10%). Seventy-one patients (53%) had no identified primary focus. In most cases (70%), the infection in the vertebral column was located in the lower part (T12-S5) (Table 4). The localization of osteomyelitis was not related to age (data not shown). Seven patients (5%) had endocarditis and 3 patients (2%) had meningitis (Table 4). One of the patients had both endocarditis and meningitis.

SIGNS, SYMPTOMS, AND LABORATORY FINDINGS

The symptoms at presentation were dominated by relatively unspecific symptoms, such as pyrexia (97%), sleep disturbances (93%), anorexia (53%), and back pain (83%) (Table 5). Pain was severe in most cases and 38 (36%) of 105 received morphines. Eighty-five percent had impaired movement, 27% had reflex disturbances, and 12% had urinary incontinence (Table 5). The ESR was increased in 98% of the cases, white blood cell counts were elevated in 64%, neutrophils (>80%) were increased in 39%, and alkaline phosphatase levels were elevated in 62% of the indicated cases (Table 5). Medians (ranges) for ESR and white blood cell counts were 90 mm/h (7-143 mm/h) and 13.0 3x10^9/L (0.2-30.8 3x10^9/L), respectively. Cultures of bone biopsy specimens were performed in 40 cases (31%). Twelve (30%) of these specimens were obtained during open surgery, and 28 (70%) via fine needle aspirations. Cultures of these were positive for organisms in 16 cases (40%). Lumbar puncture was performed in 28 cases (21%), in which Staphylococcus aureus was cultivated in 3 cases (11%).

RADIOLOGICAL METHODS AND BONE SCINTIGRAPHY

Conventional radiography was performed in 120 (90%) of the cases. This radiological method was used only once in 59 cases (49%), twice in 39 cases (33%), and 3 or more times in 22 cases (18%). Twenty-four patients (20%) had 2, 55 patients (46%) had 3, 18 patients (15%) had 4, and 3 patients (3%) had 5 abnormal radiographic findings. Findings of conventional radiography were normal in 20 cases (17%). Of these, the diagnosis was based on re-
results of bone scintigraphy in 12 cases (60%), CT scanning in 5 cases (25%), and magnetic resonance scanning in 3 cases (15%). Among cases with abnormal results on conventional radiography, the diagnosis was confirmed using bone scintigraphy in 23 cases and CT scanning in 5 cases. The cumulative frequency of abnormal findings by different radiological methods and bone scintigraphy is illustrated in Figure 2. Abnormal radiographical findings developed late in relation to the time of onset and were present in only approximately 50% of the cases after 7 weeks. The initial findings with conventional radiography were soft tissue swelling, degenerative changes, and narrowed intervertebral disk space, while evidence of bone fusion and bone sclerosis developed much later (Figure 2). In comparison, bone scintigraphy and CT scanning produced positive results much earlier than radiography ($P<.01$) (Figure 2). Results of bone scintigraphy also seemed to be abnormal earlier compared with those of CT scanning since 80% of the cases undergoing scintigraphy were considered abnormal during the first week, while only 50% were abnormal with CT scanning (Figure 2). Results of magnetic resonance scanning were abnormal in all cases ($n=3$).

**DURATION TO DIAGNOSIS**

The duration from the first symptom to the diagnosis of osteomyelitis was a median of 46 days (range, 3–384 days) for 114 evaluable cases. Osteomyelitis was diagnosed within 4 weeks from onset in nearly half (55/114 [48%]) of the cases. For community-acquired cases, the duration from onset to admission was a median of 7 days (range, 1–367 days), and the majority (74/109 [68%]) of patients with vertebral osteomyelitis were admitted within

![Figure 2. Abnormal cases (cumulative percentage) of vertebral hematogenous osteomyelitis in Denmark for the years 1980 through 1990 diagnosed using different radiological methods and bone scintigraphy, according to duration from onset of infection. A indicates bone scintigraphy; B, computed tomographic scanning and x-ray findings; C, degenerative changes; D, narrowed intervertebral disk space; E, soft tissue swelling; F, bone sclerosis; and G, bone fusion.](image)
2 weeks. Duration from admission to diagnosis was a median of 29 days (range, 1-244 days).

Duration from admission to diagnosis could be identified in 99 (91%) of 109 community-acquired cases. Patients diagnosed less than 2 weeks after admission had a higher frequency (43/51 [84%]) of local signs or symptoms, such as impaired movement, local tenderness, or swelling, compared with patients diagnosed 2 weeks or later after admission (5/48 [10%] \( P < .01 \)). Patients with a diagnosis on admission that pointed toward an active process in the vertebrae column did not differ significantly from other patients according to time of admission or time of diagnosis from onset of symptoms (data not shown). When patients older than 60 years (n=60) were compared with younger patients (n=39), older patients experienced a longer duration from admission to diagnosis (median, 107 days; range, 14-268 days vs median, 65 days; range, 8-340 days, respectively \( P < .01 \)).

**OUTCOME**

Few patients had local spreading of the infection with abscesses in the adjoining tissue. Of 112 patients, 9 (8%) had epidural abscesses, 9 (8%) had paravertebral abscesses, and 3 (3%) had psoas abscesses. Drainage was reported in only 8 (38%) of these cases. The overall recurrence rate was 10% (13/133). Time of recurrence from the start of treatment was a median of 18 days (range, 9-70 days). Thirty-two patients (26%) developed sequelae. Of these, 21 patients (17%) had sustained pain, 14 (11%) had hypotonia and loss of mobility and reflexes, and 8 patients (7%) had either hypotonia, sensitivity loss, or loss of reflexes. Patients with sequelae differed from other patients according to age (median, 68 years; range, 12-86 years vs median, 62 years; range, 6-83 years, for those without sequelae \( P < .01 \)), and they more commonly suffered from neurological impairments when admitted (20/32 [63%] vs 31/88 [35%], respectively \( P < .01 \)). However, neither the presence of a primary focus, the vertebral localization of the infection, nor the duration from onset to start of antibiotic treatment differed between the groups of patients with or without sequelae (data not shown). Complication rates were higher for hospital-acquired cases compared with community-acquired cases (63% vs 27% \( P < .05 \)) and related to reflex disturbances and confusion \( P < .05 \). The overall mortality rate was 16% (20 of 124 patients). The mortality rate was higher (26%) for hospital-acquired cases compared with community-acquired (14%) \( P = .26 \). Duration from onset of symptoms to death was a median of 48 days (range, 7-217 days). In Table 6 certain characteristics of patients who died are compared with those of patients who survived. Patients with vascular disease of infection had a higher mortality rate compared with other patients, while patients with localized pain had a lower mortality rate (Table 6). Outcome for patients with a diagnosis on admission that pointed toward an active process in the vertebral column did not differ significantly from outcome for other patients (data not shown).

**ANTIBIOTIC TREATMENT**

The different antibiotic treatment regimens are shown in Table 7. When the outcome was evaluated, patients who died within 3 days after a positive blood culture (n=8) and patients who survived with endocarditis (n=5) and meningitis (n=1) were excluded from the analysis. Of the 8 patients who died within 3 days after a positive blood culture, 2 had endocarditis and 2 had meningitis. For sequelae and recurrences, 6 and 3 patients, respectively, were excluded because of lack of follow-up. Thus, a total of 111 and 103 patients were evaluated according to mortality and sequelae, respectively, while 114 patients were evaluated according to recurrence rate and rate of therapeutic failure.

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**Table 6. Characteristics of 124 Patients With Hematogenous *Staphylococcus aureus* Osteomyelitis**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Died</th>
<th>Survived</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y (range)</td>
<td>67 (31-85)</td>
<td>64 (6-86)</td>
</tr>
<tr>
<td>Onset to treatment, mo</td>
<td>12 (5-343)</td>
<td>11 (1-375)</td>
</tr>
<tr>
<td>Male</td>
<td>8/20 (40)</td>
<td>58/104 (56)</td>
</tr>
<tr>
<td>Community-acquired disease</td>
<td>14/20 (70)</td>
<td>87/104 (84)</td>
</tr>
<tr>
<td>Known portal of entry</td>
<td>10/20 (50)</td>
<td>49/104 (47)</td>
</tr>
<tr>
<td>Localization (T12 and below)</td>
<td>12/20 (60)</td>
<td>75/104 (72)</td>
</tr>
<tr>
<td>Recurrence</td>
<td>4/20 (20)</td>
<td>9/104 (9)</td>
</tr>
<tr>
<td>Failure of therapy</td>
<td>3/20 (15)</td>
<td>14/104 (13)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>2/18 (11)</td>
<td>3/100 (3)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>2/11 (18)</td>
<td>1/100 (1)</td>
</tr>
<tr>
<td>Elevated white blood cell count</td>
<td>12/16 (75)</td>
<td>58/89 (65)</td>
</tr>
<tr>
<td>Elevated neutrophils</td>
<td>3/5 (60)</td>
<td>18/48 (38)</td>
</tr>
<tr>
<td>Elevated ESR</td>
<td>16/16 (100)</td>
<td>99/101 (98)</td>
</tr>
<tr>
<td>Back pain</td>
<td>8/20 (40)†</td>
<td>97/101 (96)</td>
</tr>
<tr>
<td>Referred pain</td>
<td>2/20 (10)†</td>
<td>85/103 (83)</td>
</tr>
<tr>
<td>Impaired movement</td>
<td>19/20 (95)</td>
<td>85/103 (83)</td>
</tr>
<tr>
<td>Neurological problems</td>
<td>10/20 (50)</td>
<td>42/103 (41)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4/20 (20)</td>
<td>18/104 (17)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>4/20 (20)</td>
<td>12/104 (12)</td>
</tr>
<tr>
<td>IV drug abuse</td>
<td>2/20 (10)</td>
<td>4/104 (4)</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>13/20 (65)†</td>
<td>28/104 (27)</td>
</tr>
<tr>
<td>Operation</td>
<td>4/20 (20)</td>
<td>8/104 (8)</td>
</tr>
</tbody>
</table>

*ESR indicates erythrocyte sedimentation rate; IV, intravenous.
†More or less frequently \( P < .01 \) among patients who died.

**Table 7. Antibiotic Treatment and Outcome for Patients With Vertebral *Staphylococcus aureus* Osteomyelitis**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mortality</th>
<th>Sequelae</th>
<th>Failure of Therapy</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillinase-stable penicillin</td>
<td>7/51 (14)</td>
<td>15/46 (33)</td>
<td>9/50 (18)</td>
<td>10/50 (20)*</td>
</tr>
<tr>
<td>Penicillinase-stable penicillin plus fusidic acid</td>
<td>1/35 (3)</td>
<td>12/34 (35)</td>
<td>4/39 (10)</td>
<td>2/39 (5)</td>
</tr>
<tr>
<td>Other ( \beta )-lactam antibiotics</td>
<td>1/5 (7)</td>
<td>2/14 (15)</td>
<td>1/15 (7)</td>
<td>1/15 (7)</td>
</tr>
<tr>
<td>Other ( \beta )-lactam antibiotics plus aminoglycosides</td>
<td>0/5 (0)</td>
<td>1/5 (20)</td>
<td>1/5 (20)</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0/2 (0)</td>
<td>1/2 (50)</td>
<td>0/2 (0)</td>
<td>0/2 (0)</td>
</tr>
<tr>
<td>Other†</td>
<td>1/3 (33)</td>
<td>1/2 (50)</td>
<td>2/3 (66)</td>
<td>0/3 (0)</td>
</tr>
</tbody>
</table>

*Higher \( P < .05 \) compared with penicillinase-stable penicillin and fusidic acid in combination.
†Other includes rifampin plus fusidic acid, erythromycin, and chloramphenicol.
The mortality rate, recurrence rate, and rate of therapeutic failure were lower for patients treated with penicillinase-stable penicillin and fusidic acid in combination compared with those treated with penicillinase-stable penicillin alone (Table 7). However, only the frequency of patients with recurrence showed a significant difference (P<.05) (Table 7). Therapeutic failure was seen in 17 cases (14%), and of these, patients in 9 (53%) were treated with penicillinase-stable penicillin alone, 4 (24%) with penicillinase-stable penicillin and fusidic acid in combination, and 4 (24%) received other kinds of treatment (Table 7). Patients with therapeutic failure received a lower total dosage of penicillinase-stable penicillin compared with other patients (median, 98 g; range, 8-640 g vs median, 196 g; range, 21-886 g, respectively [P<.01]), and patients with recurrence had been treated for a shorter period (median, 20 days; range, 9-70 days vs median, 83 days; range, 11-90 days, respectively [P<.01]). No relation between dosage and duration of therapy was found.

The recurrence rates according to the duration of treatment for all antibiotics and patients (n=89) treated with penicillinase-stable penicillins are illustrated in Figure 3, A and B. Based on these findings the duration of treatment should be at least 8 weeks. The rate of therapeutic failure according to the total dosage of penicillinase-stable penicillins is illustrated in Figure 3, C. All patients treated with a total of 100 g or more had the same rate of therapeutic failure. The rate of therapeutic failure according to daily dosage of penicillinase-stable penicillin is shown in Figure 3, D. Based on these findings the daily dosage of penicillinase-stable penicillin should not be less than 4 g. Of these patients, 18 received intravenous therapy alone, 10 received oral therapy alone, and 61 received intravenous therapy for some weeks followed by oral therapy. Rates of therapeutic failure did not differ significantly for these small groups (data not shown). Other β-lactam antibiotics, mainly penicillins (n=5) and cefuroxime (n=13), were used less frequently either alone or in combination with aminoglycosides.

**IMMobilization PROCedURES**

Of 131 patients, 24 (18%) were treated with a corset, 8 (6%) with a body cast, and 8 (6%) with bed rest as the sole method, respectively. Nineteen patients (14%) received combined immobilization procedures. Durations of treatment were a median of 131 days (range, 24-1425 days), 90 days (range 24-180 days), and 68 days (range, 27-115 days), respectively. For these treatments it was not possible to identify major correlations with outcome.

In recent years, a rapid increase in the incidence of hematogenous Staphylococcus aureus osteomyelitis of the vertebral column has been reported. In a study of 525 cases of acute hematogenous osteomyelitis from 1959 through 1988, a shift in the localization toward the vertebral column from other bones was shown, and we recently reported that while the total number of vertebral osteomyelitis cases per 100 000 inhabitants has gradually increased since 1984, the number of hematogenous osteomyelitis cases of other bones has remained rather constant. This increase may be due to an increased number of bacteremia cases among older patients, who constitute a high proportion of all cases (median age, 65 years) (Figure 1), a finding similar in other studies. However, the number of hospital-acquired cases has also increased,
ie, 18% of the cases in this study were hospital acquired. This is in contrast to the findings of Torda et al, in which hospital-acquired osteomyelitis occurred in 60% of the patients studied. This difference may be explained by the selection criteria used. In our study only patients with hematogenous vertebral S aureus osteomyelitis were included, thus excluding all cases of postoperative osteomyelitis. Previous studies have found a male predominance but the numbers of cases in each of these studies have been low. In our study, including 133 cases, the male predominance was not obvious (53% male). The findings of a predominance of strains of bacteriophage groups I and II as well as a lower frequency of penicillin resistance relative to overall blood culture data of bacteriophage groups I and II have been low. In our study, the frequency of underlying diseases already present in the patient. Most patients had severe underlying diseases and/or conditions (Table 3). Immunosuppressive treatment and drug addiction have been reported by others as predisposing factors but were not prevalent here. Vascular disease, such as peripheral arteriosclerotic disease, was seen in 32% of the cases. Patients with diabetes have a known predisposition for pyogenic vertebral osteomyelitis, and diabetics are predisposed to infection in general and to staphylococcal infection in particular. We found alcohol abuse and/or cirrhosis of the liver in 14% of the cases, and in 6% of the cases back surgery had been performed. Vertebral bone infections occurring after spinal surgery have been reported in the literature. In 32 cases (24%) physical exercise had taken place prior to the onset of symptoms. However, nonpenetrating blunt trauma to the back is not generally considered an important predisposing factor to pyogenic vertebral osteomyelitis, despite the impression of Kulowski. As discussed by others, temporal association with the onset of vertebral symptoms is difficult and may serve to draw attention to the back or to aggravate pre-existing symptoms.

Almost all patients (97%) had pyrexia. This is a much higher frequency compared with that of other studies, which have described the presence of fever in only 21% to 50% of patients. An explanation could be that other studies also included cases other than bacteremia cases and infections with other pathogens. In common with other studies, back pain was frequently presented (83%), and tenderness (49%) has been reported by others. Sleep disturbances and anorexia were very common (93% and 53%, respectively). These are probably related to pain and fever, respectively, rather than characteristics of the disease. Referred pain was observed in 16 cases (13%). Of these, 8 had thoracic pain and 3 had abdominal pain corresponding to thoracic and lumbar osteomyelitis. In this case it should be remembered that the segmental nerves from the upper thoracic to the first lumbar segment spinal cord supply the thoracic and abdominal wall. Local swelling was only observed in 4 cases (3%). Impaired movement was present in 111 cases (85%) and always related to pain; because this symptom is subjective, evaluation is difficult. The ESR was consistently elevated (98%) and white blood cell counts were elevated in 64% of the cases. These data fit well with data from other studies and emphasize that the ESR is sensitive in detecting vertebral osteomyelitis, as described by others. On the other hand, an elevated ESR is quite nonspecific. The median ESR (90 mm/h) in this study is in the higher range compared with that of other studies. The elevated number of neutrophils was rather unspecific (39%), while elevated alkaline phosphatase levels were more specific (62%). Cultures of bone biopsy specimens were only positive for organisms in 40% of the cases, which is lower than rates in other reports. As suggested by others, a bone biopsy is critical in the absence of a positive blood culture due to sampling error and prior antibiotic therapy. Fine needle aspirations were mainly used in this study (70%), which may have a higher incidence of culture negativity compared with larger-bore cutting needles (ie, Craig needles). The majority of our patients were febrile at onset and received antibiotics when needle aspiration was performed. In addition, the selection criterion in our study was a positive blood culture, which may have excluded episodes with only positive bone biopsy results.

Duration from admission to diagnosis was longer in our study (median, 29 days) compared with the study by Torda et al (median, 11 days) probably due to a higher number of scintigraphic studies used in the latter evaluation. Based on our findings, physicians should focus on older patients (older than 60 years) with local symptoms such as impaired movement, local tenderness, or swelling. Duration from onset of symptoms to admission was, in contrast, only a median of 7 days (range, 1-367 days).

Several studies have shown a relation between vertebral infection and focus in the genitourinary tract, but some of these included cases with gram-negative pathogens. In contrast, the genitourinary tract was the primary focus in only 13% of the cases in the study by Torda et al and only 10% in our study. However, other studies have shown significance in recovering S aureus from the urine in the course of S aureus bacteremia. In our study the urinary tract was a primary focus when S aureus was cultivated from the urine and no other focus was located. However, the bacteriuria may only reflect a spillover from the blood. The majority of osteomyelitis cases (56%) with infection located in the lumbar region may be due to higher stress placed on the lower region during life. A higher blood flow to the larger lumbar bones may be another reason.

Knowledge of the development of radiological abnormalities is still limited and based on only a few cases. Ab-
normalities such as soft tissue swelling and narrowed intervertebral disk space are known to appear earlier than bone sclerosis and bone fusion. In the study by Torda et al., the most common initial abnormality was loss of disk height, and only a few patients showed bone or disk destruction. In our study, the time abnormal findings appeared in relation to the time of onset was evaluated; however, follow-up radiography was not performed in approximately half of the cases. After 4 weeks these abnormalities were visible in 30% of the cases, compared with bone sclerosis and bone fusion in 19% and 9%, respectively (Figure 2). In our study, bone sclerosis was present in 27% of the cases after 6 weeks. Degenerative changes and narrowing of intervertebral disks are findings commonly seen in patients without evidence of infection. However, of the cases (n=24) with only 2 findings considered diagnostic, bone sclerosis was found in 6 cases and a further 13 were confirmed using bone scintigraphy or CT scanning. Newer diagnostic techniques have been demonstrated to be more sensitive in detecting vertebral osteomyelitis. Bone scintigraphy and CT scanning are compared in Figure 2. It appears that both methods reveal abnormal results much earlier than conventional radiography does, and bone scintigraphy seems to detect osteomyelitis earlier. The sensitivity of bone scintigraphy in early pyogenic spondylitis is high and the specificity is low. However, low specificity is not considered to be a problem because many patients will have a blood culture positive for S. aureus, which still has to be treated with antibiotics. Evaluation of magnetic resonance scanning could not be evaluated in this study since this technique was performed only in a few cases. Patients diagnosed early had a significantly lower recurrence rate compared with other patients (P<.01), indicating that duration from onset to initiated treatment may be important. Factors such as source of infection, knowledge of portal of entry, and vertebral localization of osteomyelitis did not influence time of diagnosis. Neither did back pain, elevated white blood cell count, or elevated neutrophils. The overall recurrence rate was 13 (10%) of 133 cases, which is consistent with other studies, reporting recurrence rates varying from 3% to 40%. 5,9,19,40,53

Patients with sequelae had a higher frequency of elevated white blood cell counts (P<.01) compared with other patients and more commonly had neurological impairments when admitted (P<.01). This may be explained by their older age (P<.01). However, interpretations according to ESR are difficult to specify, especially in the elderly, because of concurrent diseases.

Twenty-two (20%) of 108 surviving patients had neurological deficits, which is a higher rate than that reported by Sapico and Montgomerie, whose study included different bacterial species known to represent different age distributions. Our study included only patients with S. aureus osteomyelitis, which may cause worse damage to the spine compared with other bacteria. The significantly higher frequency of neurological findings among diabetics as opposed to nondiabetics, as found by Sapico and Montgomerie, could not be confirmed in our present study (data not shown).

The mortality rate in our study is higher than that in another recent study but similar to the data of Norden. This relatively high mortality rate may reflect that all patients had bacteremia. The mortality rate for patients with endocarditis and meningitis was 60% (6/10). This high mortality rate for both endocarditis and meningitis has been reported in other studies (71% and 56%, respectively). 54

There are only a few studies concerning the antibiotic treatment of vertebral osteomyelitis, and recommendations from these studies are often conflicting. Intravenous therapy for at least 4 weeks is generally accepted, 22,36,48 guided by the ESR value. However, this value may be influenced by other factors aside from spinal infection and may prove difficult to interpret when the patient could have concurrent diseases. Subsequent oral antibiotic therapy is recommended for at least 3 months, while other investigators believe that if parenteral therapy has been given for 6 to 8 weeks oral therapy is not necessary. 3,41 However, these studies are based on only a few cases of osteomyelitis caused by other pathogens as well as S. aureus. Our retrospective study of 133 cases of vertebral S. aureus osteomyelitis allowed us to focus in more detail on treatment. For all treatment regimens it seems that patients with S. aureus hematogenous osteomyelitis should be treated for 8 weeks or more (Figure 3, A). These findings were independent of dosage therapy. The high number of patients treated with penicillinase-stable penicillins with or without the addition of fusidic acid were evaluated according to mortality rate, sequelae rate, rate of therapeutic failure, and recurrence rate (Table 7). Penicillin used in this study was primarily penicillin G, and penicillinase-stable penicillins included dicloxacillin and methicillin, which have been shown to be equivalent in potency in vitro. 37 Patients who developed a recurrence had received a shorter duration of treatment with penicillinase-stable penicillins compared with other patients. Based on the curve in Figure 3, B, the duration of the treatment should be at least 8 weeks. Patients in whom therapy failed received lower antibiotic dosages compared with those of other patients.

Based on the findings in Figure 3, D, it seems reasonable to recommend at least 4 g of penicillinase-stable penicillins per day and a total dosage of at least 100 g (Figure 3, C) (it was not possible to obtain the body weight based on the patients’ data). This finding was independent of the duration of therapy. When comparing treatment with penicillinase-stable penicillins there was a nonsignificant (P=.18) lower mortality rate for the regimen with fusidic acid (Table 7) and nearly the same rate of sequelae. The recurrence rate was significantly lower for patients treated with penicillinase-stable penicillin and fusidic acid in combination compared with those treated with penicillinase-stable penicillin alone (Table 7). Studies from the 1960s56,57 indicated that fusidic acid was effective in the treatment of acute osteomyelitis and staphylococcal infections. Several reports68-69 during the last 25 years have shown that fusidic acid is a useful adjuvant for acute bone infection, including neonatal osteomyelitis,62 and acute osteomyelitis involving other sites such as the clavicle63 and the pubis.64 We have also found that combination therapy with fusidic acid may be synergistic in the treatment of S. aureus meningitis.64 Because of the high risk of jaundice, oral administration of fusidic acid is recommended.65 It was not possible to make any recommendations for drugs other than penicillinase-stable penicillins because of the limited number of patients in those groups. None of our patients received third-generation cephalosporins.

Drainage was reported in only 38% of the cases involving abscess formation. However, since this was a retrospec-
tive study, drainage may have been performed for the residual group also. The use of bed rest and immobilization methods, such as traction, a body cast, or body brace, were used in 59 cases (+4%), which is fewer patients compared with the study by Sapico and Montgomery. As noted by Torda et al,19 bed rest and immobilization with a brace were previously thought to be important,10,20,29,32,35 but these treatments are now rarely recommended14,36,50,58 and the present study could not elucidate the value of such therapy.

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