

Vertebral osteomyelitis in northern Spain. Report of 62 cases

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Abstract

Objective

The records of 62 patients with clinical and radiographic evidence of vertebral osteomyelitis and positive bacteriological diagnosis, seen between 1979 and 1996, were reviewed in order to gather data on the epidemiology and the clinical pattern displayed by patients with this condition in northern Spain.

Results

Staphylococcus aureus (15 cases), Mycobacterium tuberculosis (15 cases) and Brucella melitensis (13 cases) were the microorganisms most frequently found in our patient series. After improvement of the sanitary and hygienic control of food products, the role of Brucella melitensis is decreasing as a causative agent (only 3 cases in the last 6 years). Staphylococcus epidermidis, present in 4 cases (6.6%), should be suspected in elderly patients with previous intravenous cannulations (3 of 4 cases).

The most frequent risk factors were alcoholism (7 cases), chronic hepatic disease (7 cases), diabetes (6 cases) and previous surgery (6 cases). Delay in diagnosis was high (the mean number of days between the onset of symptoms and diagnosis was 125). The lumbar region was the most commonly affected site. Neurologic involvement was present in 10 patients on admission (16%). ESR was > 50 mm/hr in a high number of cases. Blood cultures were found to be the most valuable routine test. Plain x-rays were normal in 10 patients (16%); in 6 of them Staphylococcus aureus was the responsible organism. Other imaging modalities showed a high sensitivity. Surgical drainage was necessary in 12 individuals (in 7 due to Mycobacterium tuberculosis). Outcome was good in the majority of cases: only 2 patients with associated endocarditis died. Neurologic sequelae were present in another 3 patients.

Conclusion

Vertebral osteomyelitis can be caused by a variety of pathogens. Therefore, bacteriological studies are necessary to establish the etiologic diagnosis and determine the specific antimicrobial treatment required.

Key words

Vertebral osteomyelitis, Staphylococcus aureus, Mycobacterium tuberculosis, Brucella melitensis.

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Introduction

Vertebral osteomyelitis (VO) is an infectious disease that affects the vertebral body and adjacent intervertebral disks; it usually appears after hematogenous spread of the infection. *Staphylococcus aureus* is the most widely represented pyogenic organism (1-6). In endemic areas, *Mycobacterium tuberculosis* and *Brucella melitensis* must also be considered as possible causative agents of the process (7).

The aim of our study was to analyse clinical data, laboratory tests, x-rays and the outcome of patients with hematogenous VO, comparing the data between different etiological groups in Spain, a country with a recognized high number of cases of tuberculosis (8) and brucellosis (9).

Patients and methods

Between 1979 and 1996, 103 cases of vertebral osteomyelitis were diagnosed at the rheumatology units of NS Aranzazu Hospital and M. de Valdecilla Hospitals in northern Spain. In 62 of them the causative agent was found. The characteristics reviewed in these 62 patients with VO of confirmed aetiology included: age, sex, risk factors for developing VO (medical history of tuberculosis, brucellosis, intravenous drug use, human immunodeficiency virus [HIV] infection, neoplasm, renal insufficiency, diabetes, chronic hepatic disease, alcoholism, use of corticosteroids or other immunosuppressive drugs, previous intravenous access devices, surgical procedures or genitourinary manipulations), number of days between the onset of symptoms and the diagnosis, location of the spine infection, fever, bacteriologic diagnostic methods, laboratory tests (ESR, white blood cell counts, haemoglobin), the presence of neurologic involvement, treatment and outcome.

Diagnosis was made on the basis of: (i) compatible signs and symptoms, including back pain with or without neurologic involvement, fever, constitutional symptoms, pain and limitation of motion on examination; (ii) typical changes on simple x-rays, computed tomography (CT) or magnetic resonance imaging (MRI); and (iii) the isolation of a causative agent in blood cultures (two or more) or sam-

ples obtained by bone biopsy, disco-vertebral needle-guided aspiration or open surgery. We accepted as positive results: (i) for *Mycobacterium tuberculosis*, isolation of the organism in other tissues or fluid samples; and (ii) for *Brucella spp.*, positive seroagglutination at a titer > 1/160. The data were compared between the three groups with a high number of cases (*Staphylococcus aureus*, *Mycobacterium tuberculosis* and *Brucella melitensis*).

The chi-square test, Student's test and Kruskal-Wallis test were used. P values < 0.05 were considered significant.

Results

The mean age of our VO patients was 57 years (range 14 - 84 years). Thirty-seven (59.7%) were male and 25 (41.3%) were female. The average follow up period was 6.2 years (range 1 - 17 years). A previous history of tuberculosis was present in 13% (2/15) of the patients with tuberculous VO. Of the patients with brucellar VO, 77% (10/13) lived in rural areas, 46% (5/13) were cattle workers, and 69% (9/13) habitually consumed unfermented fresh milk and cheese. Other risk factors identified in 27 patients (43.5%) are summarized in Table I. Alcoholism (7 cases), chronic hepatic disease (7), diabetes (6) and previous surgery (6) were the most frequent factors. The organisms isolated and the diagnostic methods used are shown in Table II. Material from the disco-vertebral lesion was obtained by bone biopsy, guided-needle aspiration or open surgery in 24 patients: culture was positive in 15 of

Table I. Risk factors identified in 27 patients.

Risk factor	No. of cases
Alcoholism	7
Chronic hepatic disease	7
Diabetes	6
Previous surgery	6
Previous i.v. cannulation	3
Renal insufficiency	2
HIV-positive i.v. drug addict	2
Neoplasm	2
Corticosteroids	2
HIV-positive non-i.v. drug addict	1

HIV: Human immunodeficiency virus.

Table II. The microorganisms isolated and the diagnostic methods used.

Organism (n = 62 patients)	Diagnostic method
<i>Staphylococcus aureus</i> : 15 pts.	Blood culture (13 pts.) Bone biopsy* + blood culture (2 pts.)
<i>Mycobacterium tuberculosis</i> : 15 pts.	Bone biopsy (8 pts.) Other cultures (5 pts.) Bone biopsy + other cultures (2 pts.)
<i>Brucella melitensis</i> : 13 pts.	Blood culture + serology (6 pts.) Serology (6 pts.) Other cultures + serology: (1 pt.)
<i>Escherichia coli</i> : 7 pts.	Blood culture (3 pts.) Blood culture + other cultures (3 pts.) Bone biopsy (1 pt.)
<i>Streptococcus</i> : 5 pts.	Blood culture (5 pts.)
<i>Staphylococcus epidermidis</i> : 4 pts.	Bone biopsy + blood culture (2 pts.) Blood culture (2 pts.)
<i>Pseudomona aeruginosa</i> : 1 pt.	Blood culture (1 pt.)
<i>Haemophilus influenzae</i> : 1 pt.	Blood culture + other cultures (1 pt.)
<i>Escherichia coli</i> + <i>Proteus mirabilis</i> : 1 pt.	Blood culture + other cultures (1 pt.)

*Bone biopsy, local aspiration or material obtained by open surgery.

them (62%). In the 4 patients with infection due to *Staphylococcus epidermidis* three or more cultures were positive. All 4 were elderly individuals and in 3 of them previous intravenous cannulations were present. Immunosuppression was evident in 3 of the cases; 2/4 patients suffered from a prostatic carcinoma and one was being treated with methotrexate (7.5 mg/week) and prednisone (7.5 mg daily) for rheumatoid arthritis.

The mean number of days between the onset of symptoms and the diagnosis was 125 (range 1 - 620). Inflammatory pain was present in 44 (71%) patients. Fever before admission was reported by 36 of 54 (66%) individuals. Fever during hospitalisation was present in 72.5% (45/62).

The sites at which VO was documented were lumbosacral in 42 patients, dorsal in 18 and cervical in 2. In 5 cases (2 *Staphylococcus aureus*, 2 *Mycobacterium tuberculosis* and one *Brucella melitensis*) several sites were involved. Neurological involvement on admission was present in 10 cases (16%); the isolated organisms were *Mycobacterium tuberculosis* (5 cases), *Staphylococcus aureus* (3 cases), *Brucella melitensis* (1 case)

and *Streptococcus agalactiae* (1 case). The mean ESR was 72 mm/hr (range 12-120 mm/hr), leukocyte count 8.4 10⁹/l (range 4.2 - 16.5 10⁹/l and haemoglobin 116 g/l (range 87 - 145 g/l). Simple x-rays were normal in 10 cases (16%): in 6 of them *Staphylococcus aureus* was the responsible organism, in two *Brucella melitensis*, and in one case each *Escherichia coli* and *Streptococcus agalactiae*. ^{99m}Tc scintigraphy was performed in 20 patients, ⁶⁷Ga scintigraphy in 6, CT in 23 and MRI in 27, with 19 (95%), 4 (75%), 21 (87%) and 26 (92.6%) positive results respectively.

Patients with tuberculous VO were initially treated with a combination of rifampin (10 mg/kg/day), isoniazid (5 mg/kg/day) and ethambutol (15 mg/kg/day). After 3 months of this treatment, the patients were given rifampin and isoniazid alone for 8-12 months (median total duration 12 months). The cases of brucellosis were treated with a 3-month course of oral doxycycline (200 mg/day) plus rifampin (900 mg/day). VO due to *Staphylococcus aureus* was treated with intravenous cloxacillin (2 gr every 6 hrs) for 2 weeks, followed by oral cloxacillin (1 gr every 6 hrs) for 10 weeks. The patients with other pyogenic infections

received specific (after antibiograms) i.v. induction treatment for 2 weeks, followed by oral maintenance therapy: the mean total duration of this treatment was 3.2 months (range 1.6 - 4.2 months). No relapses were documented.

Surgical drainage was necessary in 12 cases (7 due to *Mycobacterium tuberculosis*, 3 to *Staphylococcus aureus*, 1 to *Brucella melitensis* and 1 to *Streptococcus agalactiae*) because of: (i) the new presence or a worsening of neurologic involvement (3 *Staphylococcus aureus*, 3 *Mycobacterium tuberculosis*, 1 *Brucella melitensis*); (ii) large size of the abscess (1 *Streptococcus agalactiae*, 1 *Mycobacterium tuberculosis*); or (iii) involvement of the psoas muscle (3 *Mycobacterium tuberculosis*).

Neurological involvement was present one year after treatment in one patient who received only antimicrobial drugs (*Staphylococcus aureus*) and in two patients who required surgical drainage (*Mycobacterium tuberculosis*). One year after treatment mild or moderate back pain was reported by 16 patients being treated only with antimicrobial drugs and by 8 patients who underwent surgery. Static problems with kyphotic deformities were present in 5 cases of tuberculous origin. Two individuals suffering from associated endocarditis died after surgical procedures (1 with *Staphylococcus epidermidis* and 1 with *Streptococcus agalactiae* associated VO).

Table III compares the data for the patients with VO due to *Staphylococcus aureus*, *Mycobacterium tuberculosis* and *Brucella melitensis*. The delay in diagnosis was high in all patients. Fewer patients in the group with VO of tuberculous origin had fever compared to the other groups. Simple x-rays were normal in 40% of the patients with VO due to *Staphylococcus aureus*. Surgical drainage was necessary in a high percentage of the tuberculous VO patients. The remaining data did not show any statistically significant differences.

Figure 1 shows the relationship between the three groups and the years of our study. *Brucella melitensis* was the only decreasing category in the last 6 years.

Discussion

Hematogenous VO is an uncommon in-

Table III. Comparative data on the three causative agents most frequently found in our patient series.

	<i>Staphylococcus aureus</i>	<i>Mycobacterium tuberculosis</i>	<i>Brucella melitensis</i>
M/F	11/4	9/6	8/5
Age (years)	48 (16-69)	50 (19-84)	60 (43-77)
Risk factors	8/15	3/15	3/13
Fever before the admission*	9 (60%)	4 (27%)	10 (77%)
Fever while in hospital**	14/15 (93%)	6/15 (60%)	10/13 (76%)
Days between the onset of symptoms and the diagnosis&	43	218	118
Laboratory tests			
ESR (mm/hr)	90	56	53
Hemoglobin (g/l)	120	120	113
Leukocytes (10 ⁹ /l)	10.4	7.38	6.59
Location			
Cervical	1	0	1
Dorsal	5	5	2
Lumbar	9	10	10
Abnormal simple x-rays &&			
Narrowing of the disk	9/15	14/15	11/13
Adjacent lysis of bone	9/15	14/15	11/13
Adjacency lysis of bone	6/15	8/15	8/13
Sclerosis	2/15	5/15	3/13
Soft tissue extension	2/15	3/15	1/13
Osteophytosis	4/15	1/15	3/13
Abnormal imaging modalities			
⁹⁹ Tc bone scan	6/7	1/3	1/1
CT	4/5	8/15	
MRI	9/11	6/7	3/3
Surgery [§]	3/15	7/15	1/13

* p (Fisher's test) = 0.0058, comparing the M. tuberculosis group with the St. aureus + B. melitensis group.
 ** p (Fisher's test) = 0.0089, comparing the M. tuberculosis group with the St. aureus + B. melitensis group.
 & p (Kruskall-Wallis test) = 0.018 comparing the St. aureus group with the M. tuberculosis + B. melitensis group.
 && p (Fisher's test) = 0.048 comparing the St. aureus group with the M. tuberculosis + B. melitensis group.
 § p (Fisher's test) = 0.011 comparing the M. tuberculosis group with the St. aureus + B. melitensis group.

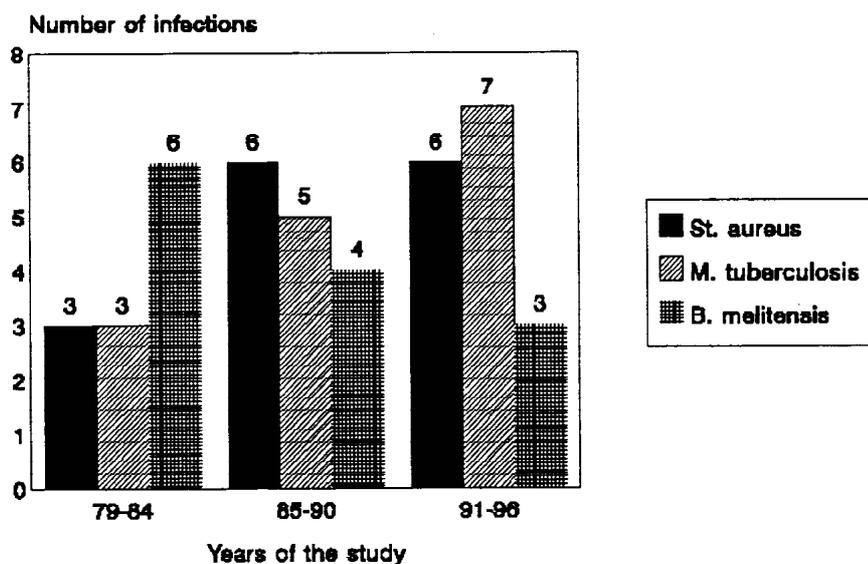


Fig. 1. Comparative data on the three microorganisms most commonly found in our patient series.

fectious entity, although in recent years its presence seems to be increasing. In our series, *Staphylococcus aureus*, *Mycobacterium tuberculosis* and *Brucella melitensis* were the organisms most commonly found. *Staphylococcus aureus* is the most frequent microorganism isolated in the majority of studies. Tuberculous spondylitis remains common worldwide (10) and Spain is a country with a high number of cases of tuberculosis, although current data regarding its incidence and prevalence are not available (8). Brucellosis is endemic in Mediterranean areas and has been documented extensively. VO was present in 38 (14%) of 265 cases of brucellosis recently reported by Colmenero *et al.* (11). In Spain, after improvement of the sanitary and hygienic control of food prod-

ucts involved in the transmission of microorganisms (mainly the production and distribution of unfermented fresh milk and cheese), the frequency of brucellosis is decreasing; its annual incidence was 22 per 100,000 in 1983 and 8 per 100,000 in 1991 (9). Our data confirm this finding.

Surgical procedures and genito-urinary procedures underlay the majority of infections due to Gram negative organisms. Interestingly, the only 4 infections caused by *Staphylococcus epidermidis* were in elderly patients. Immunosuppression (prostatic neoplasm and rheumatoid arthritis treated with low doses of prednisone) was also present in 3 of these 4 patients. Haemodialysis in diabetic patients (12), i.v. drug abuse (13), and (as in the case of 3 of our patients) intravenous cannulations in elderly patients (3), are recognized predisposing factors for the development of hematogenous VO due to *Staphylococcus epidermidis*. The increasing use in recent years of intravascular devices by clinicians in different fields has been accompanied by significant morbidity and mortality associated with catheter-related sepsis (14); one of our 4 patients suffered from an associated endocarditis and died.

Delay in diagnosis is probably correlated with the vague symptoms typical of VO and with the high incidence of back pain in the general population. Furthermore, fever was not present in 27.5% of our cases (40% of tuberculous origin). Alcoholism, chronic hepatic disease, previous surgery and diabetes were the most highly represented risk factors in our group, as in other reported series.

Culture of disco-vertebral material obtained by biopsy, local aspiration or open surgery was positive in 62% of our cases. Perronne *et al.* reported 70% positive cultures from purulent fluid obtained by local aspiration with a Laredo-Bard type needle (15). Blood cultures are the most valuable routine tests. They were positive in 33 of 34 patients with non-tuberculous, non-brucellar VO and in 46% of the brucellar infections in our study. Serology was positive in all 13 patients with brucellar VO.

The lumbosacral region is the most commonly affected site in patients with bac-

terial VO, followed by the thoracic and cervical regions. Spinal tuberculosis, however, seems to be more frequent in the thoracic segment (7, 16). The ESR is frequently greater than 50 mm/hour. 84% of our patients had abnormal plain x-rays on admission; this percentage is correlated with the delay in diagnosis. *Staphylococcus aureus* was responsible for the infection in 60% of our patients with normal x-rays. MRI seems to be the best imaging modality for the diagnosis of VO (17, 18), although good results have also been reported with CT (19).

Furthermore, MRI can show neurological compression of the spinal cord, and paravertebral and/or epidural extension of the infection (18).

Neurological involvement, present in 16% of our cases, is an important complication of VO. It has been reported in 4% to 40% of patients in other series (2). Surgical intervention with anterior spinal debridement is indicated for patients with severe neurologic deficit, or when an abscess of large size is present, instability becomes a factor, or the medical treatment fails (20-22). Surgery was nec-

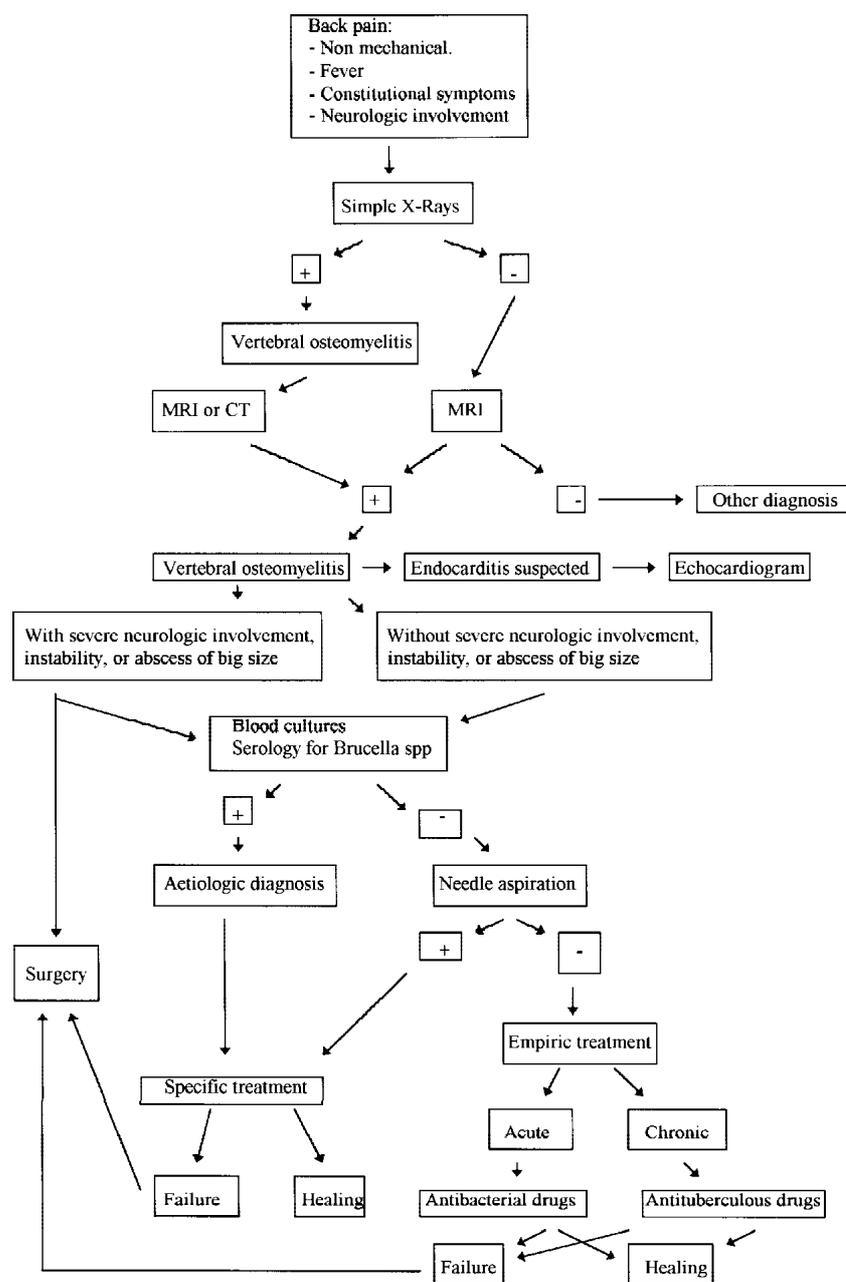


Fig. 2. Algorithm for the diagnosis and management of vertebral osteomyelitis.

essary in 19% of our patients. The need for surgical treatment seems to be less frequent in patients with brucellar VO (only one patient in our study) than in the groups with VO of pyogenic and tuberculous origin (7). In 3 of our cases of tuberculous VO, surgical drainage was necessary because of the presence of a psoas abscess, a well recognized complication of Pott's disease.

The outcome of patients with vertebral osteomyelitis is usually good despite frequent delays in diagnosis, and most patients with neurologic deficit recover. However, static problems are not uncommon, especially in patients with Pott's disease (7, 23). Mild or moderate residual back pain is also frequent after the completion of therapy. The association between VO and bacterial endocarditis has been widely described in the literature (24, 25). The latter was the cause of death in two of our patients. Therefore, a complete physical examination and inquiry for a previous history of heart disease or murmurs are also necessary. Echocardiograms must be carried out when endocarditis is suspected.

We conclude that VO is a serious medical problem. Microbiological investigations (blood cultures, serology for *B. melitensis*, needle aspiration) are necessary to establish the etiology and select the most appropriate antimicrobial treatment. Figure 2 shows an algorithm for the diagnosis and management of VO.

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