EXTENDED REPORTS

Pyogenic, tuberculous, and brucellar vertebral osteomyelitis: a descriptive and comparative study of 219 cases

J D Colmenero, M E Jiménez-Mejías, F J Sánchez-Lora, J M Reguera, J Palomino-Nicás, F Martos, J García de las Heras, J Pachón

Abstract

Objectives—To describe a large series of patients with vertebral osteomyelitis (VO), and to compare the clinical, biological, radiological, and prognostic features of pyogenic (PVO), tuberculous (TVO), and brucellar vertebral osteomyelitis (BVO).

Methods—A retrospective multicentre study, which included 219 adult patients with VO with confirmed aetiology, who were diagnosed between 1983 and 1995 in two tertiary care centres. Of these patients, 105 (48%) had BVO, 72 (33%) PVO, and 42 (19%) TVO.

Results—One hundred and forty eight (67.6%) patients were male and 71 (32.4%) female. The mean (SD) age was 50.4 (16.4) years (range 14–84) and the mean (SD) duration of symptoms before the diagnosis was 14 (16.8) weeks. In 127 patients (57.9%) the vertebral level involved was lumbar, in 70 (31.9%) thoracic, and in 16 (7.3%) cervical. One hundred and nineteen patients (54.4%) received only medical treatment and 100 (45.6%) required both medical and surgical treatment. The presence of diabetes mellitus, intravenous drug abuse, underlying chronic debilitating diseases or immunosuppression, previous infections, preceeding bacteraemia, recent vertebral surgery, leucocytosis, neutrophilia, and increased erythrocyte sedimentation rate (ESR) were significantly associated to PVO. A prolonged clinical course, thoracic segment involvement, absence of fever, presence of spinal deformity, neurological deficit, and paravertebral or epidural masses, were significantly more frequent in the group of TVO. The need for surgical treatment and the presence of severe functional sequelae were more frequent in the groups of PVO and TVO.

Conclusion—There are significant clinical, biological, radiological, and prognostic differences between BVO, PVO, and TVO. These differences can point to the causal agent and orient the initial empiri-

cal medical treatment while awaiting a final microbiological diagnosis.

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In 1975 Ross and Fleming rightly pointed out “neither common enough to be readily recognizable, nor rare enough to be a medical curiosity, vertebral osteomyelitis (VO) represents a diagnostic challenge to the physician”.¹ The clinical picture of VO is rather non-specific. It commonly starts insidiously and follows an indolent course making early diagnosis difficult.^{2–4} Consequently, patients often develop highly destructive lesions or neurological complications related to compression of the spinal cord or its roots.⁵

Most of the published series of VO have limited their scope to the description of cases or to a detailed analysis of particular aetiological categories or risk factors.^{1–4 6–9 10–13} In many parts of the world, and in Mediterranean countries particularly, both brucellosis and tuberculosis still have a high incidence. However, there is no study that compares the clinical, radiological, and prognostic features of pyogenic, brucellar, and tuberculous vertebral osteomyelitis.

Given the fact that an aetiological diagnosis is not always obtained even when invasive techniques are used,^{2–4} and that the therapeutic strategy varies widely depending on the causal agent, the establishment of criteria that could help to distinguish between aetiological groups is of importance.^{14–16}

The aim of this study is to describe the clinical and evolutive features of a large series of cases of VO, with particular attention to the differential aspects of the three most frequent aetiological groups in Mediterranean countries.

Methods

STUDY POPULATION

All patients older than 14 years of age who had a diagnosis of VO between January 1983 and December 1995 in the University Regional Hospital “Carlos Haya” of Málaga and the

Unit of Infectious Diseases, University Regional Hospital “Carlos Haya”, Málaga, Spain
J D Colmenero
F J Sánchez-Lora
J M Reguera
F Martos

Unit of Infectious Diseases, University Hospital “Virgen del Rocío”, Seville, Spain
M E Jiménez-Mejías
J Palomino-Nicás
J García de las Heras
J Pachón

Correspondence to:
Dr JD Colmenero, Unit of Infectious Diseases, Internal Medicine Department, Hospital Regional de Málaga, Camino de Antequera s/n, 29010 Málaga, Spain.

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Table 1 Consecutive organisms isolated from 72 patients with pyogenic vertebral osteomyelitis

Bacteria	Number of cases (%)
Gram-positive cocci	40 (55.5)
<i>Staphylococcus aureus</i>	29 (40.3)
<i>Staphylococcus epidermidis</i>	9 (12.5)
<i>Streptococcus viridans</i>	2 (2.8)
Gram-negative bacilli	18 (25.0)
<i>Escherichia coli</i>	8 (11.1)
<i>Pseudomonas aeruginosa</i>	7 (9.7)
<i>Proteus mirabilis</i>	2 (2.8)
Unidentified species	1 (1.4)
Anaerobic bacteria	5 (6.9)
<i>Peptostreptococcus spp</i>	1 (1.4)
<i>Propionibacterium spp</i>	1 (1.4)
<i>Bacteroides fragilis</i>	2 (2.8)
<i>Eikenella corrodens</i>	1 (1.4)
Polymicrobial isolates*	3 (4.2)
<i>Candida albicans</i>	5 (6.9)
Other†	1 (1.4)

* One case each of *Acinetobacter baumannii*+*Enterococcus faecalis*+*Escherichia coli*, *Pseudomonas aeruginosa*+*Stenotrophomonas maltophilia*+*Prevotella melaninogenica*, *Pseudomonas aeruginosa*+*Streptococcus spp*+*Bacteroides fragilis*, †*Corynebacterium spp* one case.

University Hospital “Virgen del Rocio” of Seville, were included. Both hospitals are tertiary care centres, providing referral attention to two large metropolitan areas in the south of Spain with a population of 1 250 000 and 1 000 000 inhabitants respectively. Irrespective of the unit of the hospital where the patient was initially admitted, all the patients were seen and followed up by one of the authors.

INCLUSION CRITERIA AND DEFINITIONS

The diagnosis of VO was established in the presence of these two criteria: a compatible clinical picture together with one or more imaging techniques showing data compatible with spondylitis. A compatible clinical picture was defined as the presence of spinal pain with inflammatory features (pain unrelieved by rest), or fever and spinal pain on physical examination.

Imaging findings compatible with VO were considered to be one or more of those previously reported by Modic *et al*¹⁷: (a) Decreased height of the intervertebral disc with osteolysis of the end plates or adjacent vertebral bodies in plain radiographs or tomographic study. (b) The above mentioned sign detected by computed tomography (CT), with or without the presence of a soft tissue mass. (c) Hypercaptating signals involving the vertebral bodies in the region of interest, coupled with pool imagings showing hyperaemia on technetium bone scan. (d) Confluent de-

creased intensity signals from the vertebral bodies and intervertebral disc space, together with failure to distinguish an imaging between the disc and the adjacent vertebral body, on T1 weighted magnetic resonance image (MRI), and an increased signal intensity from the vertebral bodies and disk with T2 weighted magnetic resonance image.

Definite aetiological diagnosis of VO was considered when the causative microorganism was isolated from a percutaneous or open bone biopsy. Diagnosis was considered probable when a typical histopathological pattern of tuberculosis (with caseating granulomas) was observed in a bone biopsy, or when—together with a consistent clinical, radiological picture—a microorganism was isolated from blood cultures or other coexistent infectious foci, or when high serological titres of brucella antibodies or seroconversion between two samples taken two or three weeks apart were reported in patients with symptoms consistent with brucella infection. According to internationally accepted criteria, significant titres were considered to be > 1/160 for Wright's seroagglutination, > 1/100 for indirect immunofluorescence and > 1/320 for the anti-brucella Coombs test.¹⁸ Fungal VO was included in the pyogenic group.

Therapeutic failure was defined as persistent or worsening symptoms together with a high C reactive protein level or erythrocyte sedimentation rate (ESR), or worsening imaging findings, or all three, after a month of specific treatment in the cases of brucellar vertebral osteomyelitis (BVO) and pyogenic vertebral osteomyelitis (PVO), and three months in tuberculous vertebral osteomyelitis (TVO). A relapse was defined as the reappearance of symptoms not attributable to other causes, or new vertebral lesions together with raised C reactive protein level or ESR, or both, after the end of the treatment. Functional sequelae were considered severe when disability prevented the patient from the performance of their occupation or daily activities.

DATA COLLECTION

Clinical, biological, radiological, microbiological, and therapeutic data of every patient were retrospectively collected from the medical records of the patients diagnosed between 1983 and 1989. From 1990 to 1995 the data were collected prospectively according to a specifically designed protocol. The recorded

Table 2 Risk factors or conditions associated with vertebral osteomyelitis

Risk factor/associated illness	Total group number (%)	BVO number (%)	TVO number (%)	PVO number (%)	Significance
Diabetes	27 (13.3)	5 (4.8)	5 (4.9)	17 (23.6)*	p < 0.00005
IDU	13 (5.9)	1 (0.9)	3 (7.1)	9 (12.5)*	p < 0.005
Previous focal infection and/or bacteraemia	50 (22.8)	8 (7.6)	0	42 (58.3)*	p < 0.00001
Bone spine surgery	18 (8.2)	0	1 (2.4)	17 (23.6)*	p < 0.00001
Immunocompromising or debilitating diseases†	24 (10.9)	3 (2.8)*	6 (14.3)	15 (20.8)	p < 0.001

BVO: Brucella vertebral osteomyelitis, TVO: tuberculous vertebral osteomyelitis, PVO: pyogenic vertebral osteomyelitis. IDU: intravenous drugs use (six HIV infected).

* Significant difference with respect to the other groups.

† Glucocorticoid treatment (four patients), neoplasia (two prostate cancer, one breast cancer, one larynx cancer, and one rectum cancer), liver cirrhosis (three patients), alcoholism (four patients), pulmonary fibrosis (three patients). Renal transplant, chronic renal failure on haemodialysis, heat injuries, rheumatoid arthritis, and systemic vasculitis one each.

Table 3 Frequency of vertebral level involved listed according to aetiological group

Level affected	Total group number (%)	BVO number (%)	TVO number (%)	PVO number (%)	Significance
Cervical	16 (7.3)	8 (7.6)	0	8 (11.1)	NS
Thoracic	70 (32)	24 (22.8)	27 (64.3)*	19 (26.4)	p < 0.0005
Lumbar	127 (58)	68 (64.8)	14 (33.3)	45 (62.5)	NS
Multiple levels	6 (2.7)	5 (4.8)	1 (2.4)	0	NS

* Significant difference with respect to the other groups. Abbreviations as in table 2.

variables were age, sex, risk factors or associated illnesses, clinical presentations, diagnostic delay, ESR, total leucocyte and differential blood cell count, levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ -glutamyltransferase (GGT), alkaline phosphatase (AP), bilirubin, glucose, creatinine, protein electrophoresis, adenosine-deaminase (ADA), C reactive protein (CRP), and serological test for brucellosis. The radiological, microbiological, and histological features, together with the characteristics and duration of the treatment supplied and patient outcome were analysed.

TREATMENT AND FOLLOW UP

Patients with PVO received intravenous specific antibiotic treatment for the identified microorganism for at least four weeks, followed by oral treatment for four to 12 additional weeks. Patients with TVO received treatment with isoniazide, rifampin plus either pirazinamide or ethambutol, or both, at standard doses for two months, followed by isoniazide and rifampin for seven to 10 additional months. Finally, patients with BVO received streptomycin sulphate (1 g intramuscularly, daily) for 21 days plus doxycycline (100 mg by mouth, twice a day) for three months, or doxycycline (100 mg by mouth, twice a day) plus rifampin (900 mg by mouth, daily) both for three months. Patients with large soft tissue masses, cord or radicular compression, highly destructive lesions producing bone-spinal instability or those who suffered a therapeutic failure, were also treated surgically. The surgical approach was generally through an anterolateral access. Once treatment was finished patients were followed up monthly for at least six months, with careful attention for the detection of relapses and assessment of functional status.

STATISTICAL ANALYSIS

Statistical analysis of data was carried out using the statistical package SPSS 6.01 (SPSS Inc, Chicago, Michigan, licensed 1325145, Hospital Regional Málaga). After the descriptive study of the different variables, a Kruskal-Wallis test was applied for comparison of the

means and Pearson's χ^2 test for comparison of proportions. A p value of less than 0.05 was considered to indicate statistical significance.

Results

During the study period 235 patients were diagnosed of VO in both centres. In 16 cases (6.8%) an aetiological diagnosis could not be obtained and therefore they were excluded. Of the resulting 219 patients finally included in the study, 105 (48%) had BVO, 72 (33%) had PVO, and the remaining 42 (19%) had TVO. One hundred and thirteen patients (51.6%) were diagnosed between 1983 and 1989, and the remaining 106 (48.4%) from 1990 onwards. The diagnosis was definite in 56 cases (25.5%), of which nine were BVO, 16 TVO, and 31 PVO. A probable diagnosis was considered in the remaining 163 (74.5%), of which 96 were BVO, 26 TVO, and 41 PVO.

Within the group of PVO, *Staphylococcus aureus*, 29 cases (40.2%), and aerobic Gram negative bacilli, 18 cases (25%), were the most frequent aetiological agents. Table 1 shows the other causative microorganism.

One hundred and forty eight patients (67.6%) were male and 71 (32.4%) female. The percentage of male patients was 72.4% in BVO and 70.8% in PVO, versus 50% in TVO (p<0.05). The age of the patients ranged from 14 to 84 years, with a mean (SD) of 50.4 (16.4) years. Fifty six patients (25.6%) were 65 years of age or over. We did not find any differences between the mean ages of patients with BVO, PVO or TVO. One hundred and thirty four patients (61%) were from rural areas. This figure increased to 77% in patients with BVO versus 51% and 41.7% in TVO and PVO respectively (p<0.00005).

Table 2 shows the predisposing factors and associated diseases. The presence of diabetes mellitus, previous bacteraemia or localised infection, parenteral drugs abuse, chronic debilitating or immunosuppressive disease, and previous vertebral surgical procedures were significantly more frequent in patients with PVO.

The medical history proved to be of great value in suggesting the aetiological diagnosis.

Table 4 Clinical manifestations in patients with vertebral osteomyelitis

Signs and symptoms	Total group number (%)	BVO number (%)	TVO number (%)	PVO number (%)	Significance
Fever	155 (71)	88 (84)	13 (32)*	54 (75)	p < 0.00001
Chills/rigors	129 (59)	78 (74)	8 (20)*	43 (60)	p < 0.00001
Constitutional symptoms†	122 (56)	65 (62)	18 (45)	39 (71)	NS
Inflammatory spinal pain‡	203 (93)	98 (93)	38 (90)	67 (93)	NS
Spinal deformity	30 (14)	7 (7)	17 (41)*	6 (9)	p < 0.0001
Neurological symptoms	123 (56)	44 (43)	32 (76)*	44 (61)	p < 0.0001
Neurological deficits	75 (35)	20 (19)	26 (62)*	29 (41)	p < 0.0001

* Significant difference with respect to the other groups. † Two or more of anorexia, adinamia or malaise. ‡ Spontaneous spinal pain unrelieved by rest. Abbreviations as in table 2.

Table 5 Summary of haematological and biochemical data

Signs and symptoms	Total group mean (SD)	BVO mean (SD)	TVO mean (SD)	PVO mean (SD)	Significance
Leucocytes (ml)	9155 (4880)	7202 (2566)	9062 (3829)	12271 (6406)*	p < 0.00001
Neutrophils (ml)	6394 (4564)	4428 (2074)	6446 (3260)	9428 (6251)*	p < 0.00001
Haemoglobin (g/dl)	12.4 (2.2)	12.9 (2.1)	12.6 (1.9)	11.4 (2.2)	NS
ESR (mm/h)	57 (36)	43 (27)	54 (39)	81 (34)*	p < 0.00001
ALT (U/l)	52 (121)	60 (164)	55 (68)	38 (37)	NS
Alkaline phosphatase (U/l)	309 (509)	259 (115)	250 (137)	419 (875)	NS
Total protein (g/l)	69.1 (8.4)	69.2 (6.5)	68.2 (10.6)	67.9 (10.1)	NS
Albumin (g/l)	36.4 (6.6)	38.1 (5.5)	36.1 (7.1)	33.1 (7.0)*	p < 0.0005
α_2 globulin (g/l)	7.8 (2.2)	7.5 (2)	7.9 (2.1)	8.4 (2.5)	NS
γ globulin (g/l)	14.1 (5.6)	13.4 (3)	12.8 (5.0)	16.5 (7.9)*	p < 0.005
C reactive protein (mg/l)	62 (59)	58 (48)	39 (37)	73 (74)	NS

ALT = alanine aminotransferase, ESR = erythrocyte sedimentation rate. * Significant difference with respect to the other groups. Other abbreviations as in table 2.

Twenty four patients with BVO (22.9%), had a diagnosis of brucellosis during the previous year (with isolation of *B melitensis* in blood culture in eight of them), 14 (33.3%) with TVO had an active or recently diagnosed tuberculosis in another location. Forty two patients (58.3%) of the PVO group had had previous infections at other sites: 15 were skin and/or soft tissues infections, 11 urinary tract infections, four digestive infections, three non-vertebral osteoarticular infections, and nine infections at other sites. In 22 of PVO cases (30.6%) and in eight of BVO cases (33.3%) previous bacteraemia could be reported.

VERTEBRAL LEVEL

Table 3 shows the vertebral levels involved. In TVO the thoracic segment was significantly the most frequently affected level ($p < 0.00005$).

CLINICAL MANIFESTATIONS

The mean duration of symptoms before diagnosis was 14 weeks in cases without a previous surgical procedure, and 2.4 weeks in those cases associated with previous surgery. The mean (SD) diagnostic delay was 22.9 (23.9) weeks in TVO versus 14.3 (16.3) weeks in BVO and 7.1 (5.7) weeks in non-postoperative PVO $p < 0.0001$. Neurological deficits were evident in 75 cases (34.2%); 23.5% had objective sensory loss, 14.7% had impaired or absent tendinous reflexes, 19% had limb weakness, and 5.1% had paraplegia or tetraplegia. Absence of fever and chills was significantly more frequent in TVO. Conversely, this group had a significantly higher rate of spinal deformity and neurological deficits (table 4).

LABORATORY TESTS

Table 5 shows the main biological data. Total leucocyte, neutrophil counts, and ESR values were significantly higher in PVO.

IMAGING TECHNIQUE FINDINGS

All patients had a plain radiography of the spine done. Vertebral CT was performed in 139 patients (63.4%), MRI in 71 patients (32.4%) and technetium-99 bone scanning in 121 patients (55.2%). In seven patients (3.1%) the plain radiography was repeatedly normal throughout the entire evolutive course; of these seven patients, six had BVO and one had TVO. Of the patients with normal radiography, six

(85.7%) had hypercaptating signals in technetium-99 bone scan and one (14.3%) was diagnosed by MRI.

In 197 patients (89.9%) evidence of disc involvement was present in one or more imaging techniques. The mean (SD) number of involved vertebrae was 2.1 (0.8), significantly higher in TVO (2.6 (1.2)) than in BVO (2.1 (0.8)) or PVO (1.9 (0.5)) ($p < 0.002$). One hundred and eighty one patients (82.6%) had involvement not only of the end plates but also of one or more vertebral bodies. Of these patients, in 60 cases (33.3%) the lesion was anterior, in 16 (8.8%) it was exclusively posterior, and in 105 (58%) the lesion affected both the anterior and posterior vertebral body. Paravertebral masses were detected in 109 cases (49.7%), epidural masses in 80 (36.5%), and psoas abscesses in 24 (10.9%). Paravertebral or epidural masses were present respectively in 78% and 68.3% of TVO, versus 39.8% and 23.5% of BVO, and 53.5% and 40.8% of PVO ($p < 0.0005$ and 0.00001 respectively).

BACTERIOLOGICAL DIAGNOSIS

Blood culture was performed in 152 patients (69.4%). Of these, 52 were positive (34.8%). Bone biopsy was performed in 133 patients (60.7%). In 42 (31.6%) the specimen was obtained by percutaneous CT guided biopsy and in 91 (68.4%) by open biopsy. Bone biopsy culture was performed in 114 patients (52%). Of these, 56 (49.1%) were positive. Table 6 shows the yield of the different techniques.

TREATMENT AND OUTCOME

In 173 patients (79%) the treatment was specific from the beginning and in 46 (21%) the initial empirical regimen was modified when a specific aetiology of VO was confirmed. The mean (SD) duration of treatment was 63 (29) days (range 14–147 days) in PVO, 98 (48) days in BVO, and 295 (87) days in TVO. One hundred and nineteen patients (54.3%) received medical treatment only and 100 (45.7%) required additional surgery. The need for surgical treatment was indicated from the time of diagnosis in 72 cases, and in the remaining 28 it was a decided upon after the failure of medical treatment. In all the operated patients, curetage and debridement of the lesion was performed, in 82.6% of cases abscesses were drained or soft tissue masses were resected, in 47% of cases bone grafts were used, and only in 2.9% an external fixation had

Table 6 Diagnostic yield of the different microbiological techniques

Diagnostic test P/N (%)	Total group number (%)	BVO number (%)	TVO number (%)	PVO number (%)	Significance
Blood culture	57/152 (37.5)	29/70 (41.4)	0/27 (0)*	23/55 (41.8)	p < 0.0000
Bone biopsy culture	56/114 (49.1)	9/37 (24.3)	16/34 (47)	31/43 (72.1%)*	p < 0.00005
Culture of other specimens	44/63 (69.8)	4/10 (40)	8/16 (50)	32/37 (86.5%)*	p < 0.0001

P/N = number of positive results/total number of performed studies. P = positive test, N = negative test. * Significant difference with respect to the other groups. Other abbreviations as in table 2.

Table 7 Treatment and outcome of vertebral osteomyelitis

	Total group number (%)	BVO number (%)	TVO number (%)	PVO number (%)	Significance
Medical treatment	219 (100)	105 (100)	42 (100)	72 (100)	NS
Only medical treatment	119 (54.3)	70 (66.7)	10 (23.8)*	39 (54.2)	p < 0.0001
Therapeutic failure	27 (12.7)	15 (14.3)	10 (23.8)	2 (2.8)*	p < 0.005
Surgical treatment	100 (45.6)	35 (33.3)	32 (76.2)*	33 (45.8)	p < 0.00001
Relapse†	10 (4.8)	3 (2.9)	3 (7.3)	4 (5.8)	NS
Death	7 (3.2)	2 (1.9)	3 (7.3)	2 (2.8)	NS
Severe functional sequelae†	67 (32.3)	18 (18.1)*	17 (49.3)	29 (41.2)	P < 0.0001

* Significant difference with respect to the other groups. † Percentages calculated over 207 patients who completed the follow up. Abbreviations as in table 2.

to be used. Patients with TVO needed surgery more frequently than those with other aetiologies ($p < 0.00001$).

Seven patients died (3.2%); in four of them (1.8%)—two with BVO and two with PVO—death was attributable to the vertebral infection. The remaining three patients, all with TVO, died of other causes (table 7).

The mean (SD) overall hospital stay was 57 (44) days: 80 (32) days for TVO, versus 41 (38) and 61 (49) in BVO and PVO respectively ($p < 0.00001$).

The prognosis of the postoperative cases did not differ significantly from that of non-postoperative cases, although the mean (SD) overall hospital stay of the postoperative cases was 74.7 (48.2) days, significantly longer than the 51.1 (28.7) days of the non-postoperative cases, $p < 0.05$.

Five patients were lost to follow up. Of the 207 patients who completed the follow up period, 10 (4.8 %) had relapses. Of these 10 patients, seven (5.9%) had received medical treatment only and the other three (3%) had also been operated on. Sequelae were minimal or non-existent in 139 (65.2%) and severe in 67 (32.3%), the latter being significantly more frequent in the PVO and TVO groups than in BVO ($p < 0.0001$).

Discussion

Vertebral osteomyelitis is an infrequent infection.^{3 7} The information regarding its incidence is scarce.^{6 7 9} However, evidence suggests that the incidence of VO is increasing because of growing number of older patients, patients with chronic debilitating diseases and immunosuppression, and the frequent use of invasive techniques and spinal surgery.^{6 10 12 19-21} Most of the series of VO include mainly PVO cases^{1 3 6 7 9 10 19 20} are usually short, and with a high percentage of cases without a microbiological diagnosis.^{1 6 8 9 10}

In our setting we found an annual incidence of seven cases per million of inhabitants, which is higher than that reported by other authors. This high incidence rate could be explained by the particular epidemiology of our geographi-

cal setting. The two hospitals where patients were recruited are located in the south of Spain, an area where brucellosis is an endemic disease with an annual incidence in the past few years of between 13–25/10⁵ inhabitants.²¹

In Mediterranean countries and in many other world areas, brucellosis continues to be an endemic infection.²³⁻²⁵ In adults, brucellosis produces VO in 6% to 12% of cases.^{18 26 27} In most of these countries the incidence of tuberculosis is also high, and it has even increased in the past few years because of the HIV epidemic.^{28 29} Spinal involvement is one of the most frequent locations of extrapulmonary tuberculosis.^{30 31}

As in many other previous studies, *Staphylococcus aureus* was the most frequent isolated microorganism in PVO, followed by aerobic Gram negative bacilli.^{1 3 4 14 15} However, it is worth mentioning the considerable proportion of cases caused by polymicrobial flora, anaerobic bacteria, and *Candida albicans*. This fact, which has been scarcely reported in the medical literature, has a direct relation to the high number of patients with chronic debilitating diseases or immunosuppression in our series. In fact, all the patients in our series who had PVO caused by polymicrobial flora or *Candida albicans*, suffered chronic debilitating diseases, were immunosuppressed or had had previous spinal surgery done. In those patients with previous spinal surgery *S epidermidis* was isolated significantly more frequently than *S aureus* (data not shown).

In some studies, cases of BVO have been included in the group of PVO.^{3 14} However, previous evidence suggests that the clinical course and prognosis of BVO are quite different to those of PVO and TVO.^{16 32 33}

The mean age in our series was similar to that reported by other authors, with a high percentage of cases occurring in patients older than 65 years.^{3 4 6 14 15} We could not find differences of age between the different aetiological groups.

The association of diabetes mellitus, intravenous drugs abuse, focal infections or bacteraemia and surgery with PVO has been reported in many studies.^{3 4 12-15 34} This study confirms

those associations and highlights their discriminative value to distinguish PVO from the other two aetiological groups.

Thoracic involvement was significantly more frequent in TVO, which may be explained by the frequent involvement of mediastinal lymph nodes and the pleura in pulmonary tuberculosis, from where microorganism can reach the vertebral bone through the lymphatic route.³⁵

The clinical picture of VO is rather non-specific. Spinal pain and paravertebral muscle spasm are, by far, the most common clinical findings.^{3 6 9 13 14 16 19} Notably, fever is often absent, even in the group of PVO, which frequently makes clinicians rule out the possibility of infection. In this study 30% of patients had no fever. The absence of fever was significantly more frequent in the group of TVO. Conversely, spinal deformity was significantly more frequent in this group. This fact is in close relation to the considerable destructive character of caseating granuloma, and it is an important diagnostic clue when present.^{15 35 36}

The mean diagnostic delay was 14 weeks, similar to the largest reported series.^{5 14} The diagnostic delay was significantly shorter in PVO, which may possibly reflect the higher clinical expression of this group of patients, which permits an earlier diagnosis.^{3 14 15}

Neurological deficits were detected in 34.2% of patients, which is similar to the reported 10% to 50% rates. They were significantly more frequent in TVO. The larger diagnostic delay and the frequent existence of spinal deformity, partially explain this fact.^{14 16 36 37}

The usual haematological and biochemical parameters are of little value in the diagnosis of VO.^{1 3 4 6-9 13-15} Our study confirms this fact. However, when leucocytosis, neutrophilia, and very high values of ESR and C reactive protein are present, they strongly suggest PVO.¹⁵

Computed tomography and MRI have significantly improved the sensitivity and specificity of simple radiography in the diagnosis of VO.^{13 38-42} It was not the purpose of our study to analyse the yield of the different imaging techniques in VO. However, we found that some findings may be helpful in distinguishing the three main aetiological groups. In this respect, thoracic level involvement, lesions affecting the posterior portion of the vertebral body, and the existence of paravertebral or epidural soft tissue masses should point to infection by *Mycobacterium tuberculosis*.^{38-40 43}

Aetiological diagnosis of vertebral osteomyelitis is frequently difficult, requiring in 30 to 70% of cases the performance of percutaneous or surgical vertebral bone biopsies.^{1 3 4 8 9 13 15}

The percentage of cases with an aetiological diagnosis in our series (93.2%) is higher to that reported by most of the previous studies. This could be explained by the higher incidence of VO in our setting, which results in a high suspicion index.

As reported by previous studies^{3 6 13 14 19} blood culture was the most useful routine test, resulting in the isolation of the responsible microorganism in 33% of patients from whom it was obtained: 41.4% in BVO and 41.8% in PVO. The yield of routine bacteriological and

serological tests was very high in BVO; in only five cases (4%) bone biopsy was necessary for the diagnosis, which is similar to other brucella spondylitis case series.^{18 26 27} In contrast, bone biopsy was necessary to establish the diagnosis in 50% of PVO and almost 75% of TVO.^{4 13 14 19}

The prognosis of VO depends strongly on an early diagnosis, the identification of the causal agent, and the initiation of a specific treatment.^{3 4 7-15 20} The results of this study are in contrast with those that consider VO an infection with a good prognosis, which usually requires only medical treatment.^{6 7 9 44} We think, as other authors do, that spondylitis is a potentially dangerous infection.^{3 5 19 45} The attributable mortality and the percentage of relapses in our study are similar to those reported by previous series.^{3 18 46} However, the need for surgical treatment in 45% of cases, and the presence of severe functional sequelae in up to 35% of cases, are higher than previously reported rates, which range between 10% to 25%,^{8 10 14 19} and 5% to 15% respectively.^{1 3 6 10} These figures are even more surprising if we consider that 48% of cases of our series were BVO, which, as can be concluded from our study, has a better prognosis than that of the other two groups.

The frequent need for surgery and high rate of functional sequelae found in our study cannot be attributed to a longer diagnostic delay or to the therapeutic regimens used, nor to the hospitals where patients were diagnosed and treated. The diagnostic delay in this study is similar to that reported by other authors, and even shorter than that reported by some series with better final prognosis.^{4 14 15} On the other hand, the therapeutic schemes, indications for surgery and surgical techniques were those that are internationally accepted.^{3 8 10 13 14 19 20 27-29} Finally, most of the published series are also based on referral hospitals.^{1 3 5 7-10 13-15 26}

In summary, our study provides evidence that there are significant clinical, biological, radiological, and prognostic differences between BVO, PVO, and TVO. These differences point to the causal agent and can suggest the empirical medical treatment, which should only be started once blood cultures, and eventually bone biopsy, have been obtained. Irrespective of the causal agent, VO is a serious infectious disease, which frequently requires surgical treatment, and produces severe functional sequelae and long hospital stays.

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