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ORIGINAL ARTICLE

Vertebral osteomyelitis: eight years' experience of 100 cases

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Abstract To evaluate the etiology and characteristics of vertebral osteomyelitis cases in our country, patients with vertebral osteomyelitis between January 2000 and December 2007 were included in this study. Clinical and laboratory data of the patients were collected from the medical records retrospectively. Of these 100 patients, 44 had pyogenic, 24 had brucellar, and 32 had tuberculous spondylodiscitis. The age of the patients ranged from 13 to 82 years, with a mean of (SD±) 55 ± 15.6 years. Within the pyogenic group, 10 (22.7%) patients had a spinal surgery history, and in 18 patients of the pyogenic group, an etiological agent was isolated. Ten (56%) of these 18 were methicillin-sensitive *Staphylococcus aureus*. While all of the patients included in this study suffered from pain, 49 of these had fever. Sixty-nine percent of the patients had lumbar involvement. The etiological distribution may differ according to geographical areas. Although brucella and tuberculosis (TB) are endemic in our country, pyogenic vertebral osteomyelitis was more frequent. The most common involved area in our patients was the lumbar vertebrae. Although thoracic involvement may be more predominant in tuberculous vertebral osteomyelitis, it does not strongly suggest TB. Magnetic resonance imaging may exclude some disorders mimicking vertebral osteomyelitis and may delineate the degree of the involvement. Microbiological and/or histopathological examination of computerized tomography-guided fine-needle aspiration biopsies are the mainstays for the diagnosis. Suspicion and early diagnosis seem critical for preventing sequelae development.

Keywords Vertebral osteomyelitis · Pyogenic · Brucellar · Tuberculous

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Introduction

Inflammation of the intervertebral disk tissue and adjacent vertebrae has been referred to as spondylodiscitis or vertebral osteomyelitis (VO), representing 2–7% of osteomyelitis cases [1, 2]. It has been divided into two major groups with regard to etiology—tuberculous and nontuberculous [1]. It is primarily a disease of adults, with the majority of patients being older than 50 years [2]. In adults, the clinical signs and symptoms may be nonspecific and early diagnosis may be difficult [3].

The lumbar vertebral bodies are most often involved, followed in frequency by the thoracic and rarely cervical vertebrae. The presentation may be acute, subacute, or chronic [4]. Localized insidious pain and tenderness in the spinal area are present in 90% of the patients. Fever is present in approximately 50% of patients. Motor and sensory deficits due to spinal cord or nerve root compression may develop [1, 4].

The most important infecting organism in pyogenic spinal osteomyelitis is *Staphylococcus aureus,* and skin, recent invasive procedures, and vascular catheters may be a portal of entry [5–7]. The second leading microorganism is *Escherichia coli*. Coagulase-negative staphylococci and *Propionibacterium acnes* are mostly involved in

osteomyelitis after spinal surgery [5, 8]. Gram-negative aerobic bacteria and *Candida spp*.-related infections are seen most commonly in intravenous drug abusers, immunosuppressed, or postoperative patients. Brucellar vertebral osteomyelitis (BVO) is common in endemic regions [1].

A culture of biopsy specimen has a higher diagnostic yield than blood cultures. Leukocyte count is increased on presentation in only approximately half of cases and does not have a high sensitivity for the diagnosis. On the other hand, increases in the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level are highly sensitive. CRP level correlates better with clinical response to treatment when compared with ESR [1, 2, 5, 9].

The most frequently used imaging modalities for the diagnosis include bone scintigraphy, radiography, computed tomography (CT), and magnetic resonance imaging (MRI). The only imaging modality that combines high sensitivity and specificity is MRI. CT-guided fine-needle aspiration biopsy (FNAB), with a sensitivity of 50%, is generally necessary to obtain a microbiology and pathology-based diagnosis [1].

The goals of therapy include eradicating the infection, relieving pain, preserving, or restoring neurological function [1].

Our aim was to describe a large series of VO in our country and to evaluate the etiologies, the characteristics of pyogenic, brucellar, and tuberculous VO, and the role of the diagnostic modalities.

Methods

One hundred patients diagnosed as VO between January 2000 and December 2007 were enrolled consecutively in this study. The diagnosis was established when a clinical picture (spinal pain and/or fever) together with one or more imaging studies and/or laboratory data (histopathological and/or microbiological) suggesting spondylodiscitis was present. Radiological diagnosis of VO was considered when one of the followings was present as reported by Modic et al. [10]: Decreased height of the intervertebral disk with osteolysis of the end plates or adjacent vertebral bodies in CT with or without a soft tissue mass; confluent decreased intensity signals from the vertebral bodies and intervertebral disk space on T1-weighted MRI; and an increased signal intensity from the vertebral bodies and disk with T2-weighted MRI [10, 11].

Diagnosis of VO was accepted as definite when a microorganism was isolated or polymerase chain reaction (PCR) for mycobacterium tuberculosis complex was positive or typical histopathological pattern of tuberculosis (TB) was observed in aspirated materials with FNAB (home-made nested PCR using primers targeting for MPB 64 protein of M. tuberculosis was performed as described by Therese et al. [12]). Diagnosis of BVO was established when high serological titers of brucella antibodies (>1/160 for Wright's seroagglutination) were reported in patients. Diagnosis was considered as probable when histopathologically inflammatory pattern that may suggest pyogenic VO (variable degrees of acute and chronic inflammatory cell infiltration, fibrosis, and vascular proliferation associated with granulation tissue in the disk tissue and adjacent vertebrae, depending on the stage of the disease; purulent inflammation with abscess formation in the patients with severe acute phase [13]) was observed in FNABs, or when together with clinical, radiological picture compatible with VO, a microorganism was isolated from blood culture or other coexistent site of infection. The probable cases were supported with their response to antibacterial treatment. Fungal VO was included in the pyogenic vertebral osteomyelitis (PVO) group.

Clinical and laboratory data of the patients were collected from the medical records retrospectively. The patients were followed-up as outpatients for 1 year after the completion of the therapy.

Statistical analysis

Data were analyzed using SPSS, version 16.0 (SPSS). Data were given mean ± standard deviation. Laboratory data and mean diagnostic delay among three groups were compared with analysis of variance (ANOVA), and Scheffe' was the post hoc test used. A P value of 0.05 was considered to be statistically significant.

Results

During this study period, 100 patients were diagnosed as VO. Of these, 44 had pyogenic, 24 had brucellar, and 32 had tuberculous VO (TVO). The diagnosis of 34% of patients with PVO and 59% of patients with TVO was accepted as definite. Fifty-nine patients were men and 41 women. The age of the patients ranged from 13 to 82 years, with a mean (SD±) of 55 ± 15.6 years (Table 1).

Within the pyogenic group, a microbiological diagnosis was established in 18 patients (41%). Ten (56%) of these 18 were methicillin-sensitive *S. aureus* (MSSA), and the remaining were as follow: two methicillin-resistant *S. aureus (*MRSA*)*, two *E. coli*, one *Salmonella enteritidis*, one *Pseudomonas aeruginosa*, one *Enterobacter cloacae,* and one *Geotrichum capitatum*. The remaining did not yield any bacteria, but the diagnosis was supported by the compatible histopathology, exclusion of brucella and TB, and response to antibacterial therapy. Ten of 44 patients in the PVO group had a spinal surgery history (Table 2).

Table 1 Classification of vertebral osteomyelitis according to the etiologies and epidemiological features

	N (%)	Mean age (years)	Sex	
			Male	Female
Pyogenic	44	60	29	15
Postoperative	10	55	7	3
Other	34	60	22	12
Brucellar	24	55	15	9
Tuberculous	32	49	15	17
Total	100	55	59	41

Table 2 Microorganisms isolated from patients with pyogenic vertebral osteomyelitis

Microorganisms	Number of cases (%)
Gram-positive cocci	
Staphylococcus aureus	12
Gram-negative bacilli	
Pseudomonas aeruginosa	1
Enterobacter cloacae	1
Salmonella enteritidis	1
Escherichia coli	2
Yeasts	
Geotrichum capitatum	1

Table 3 Risk factors associated with vertebral osteomyelitis

Risk factors	Pyogenic (%)	Brucellar (%)	Tuberculous (%)	Total (%)
Diabetes	8 (18)	1 (4)	5 (16)	14
Infection in other foci	8 (18)	0	6 (19)	14
Chronic renal insufficiency	3 (7)	0	2 (6)	5
Spinal surgery	10 (23)	0	0	10
Previous trauma	4 (9)	2 (8)	3 (9)	9
Malignancy	4 (9)	0	0	4

Table 3 summarizes the risk factors associated with spondylodiscitis. Diabetes mellitus was present in 14% of the cases, and infection in another focus was detected in 14% of all VO patients. Diabetes mellitus, infection in another focus, chronic renal insufficiency, and malignancy were present in 18, 18, 7, and 9% of PVO patients in our series, respectively.

All of the patients included in this study suffered from pain, 49 of these had fever, and 19 had neurological symptoms (Table 4).

Paraspinal abscess was present in nine (20%), epidural and/or paravertebral abscess in six (14%), draining abscesses in one (2%), and cord pressure in one (2%) of

Table 4 Clinical manifestations in patients with vertebral osteomyelitis

Signs and symptoms	Pyogenic (%)	Brucellar (%)	Tuberculous (%)	Total (%)
Pain	44 (100)	24 (100)	32 (100)	100
Fever	16 (36)	19 (79)	14 (44)	49
Limited motion	34 (70)	15 (62)	21 (66)	70
Neurological symptoms	9 (20)	1 (4)	9 (28)	19

Table 5 Frequency of affected level according to the etiologies

Affected level	Pyogenic (%)	Brucellar (%)	Tuberculous (%)	Total (%)
Cervical	3 (7)	2 (8)	0	5
Thoracic	8 (18)	5 (21)	8 (25)	21
Lumbar	32 (73)	16 (67)	21 (66)	69
Sacral	0	0	1 (3)	1
Cervico-thoracic			1 (3)	1
Multiple levels	1 (2)	1 (4)	1 (3)	3

PVO patients. Neurological symptoms were present in nine (20%) of them. On the other hand, in the TVO group, paraspinal abscess was present in 18 (56%), epidural and/or paravertebral abscess in five (16%), draining abscesses in three (9%), and cord pressure in five (16%) patients. But neurological involvement was present in nine (28%) cases.

The vertebral levels involved are shown in Table 5. Sixty-nine percent of the patients had lumbar involvement. Lumbar involvement was predominant in all three group of patients.

Excluding the postoperative PVO, source of infection was urinary system in three, osteoarticular in two, hemodialysis catheter in one, and skin in one of the patients in PVO group. Four patients with a previous surgery history were assumed to have bacteremia causing VO.

In the TVO group, seven patients (22%) reported a TB history and six patients (19%) had disseminated TB (two TB meningitis, two TB meningitis + urinary system TB, one TB pleurisy + meningitis, and one TB peritonitis).

Mean leukocyte count was (SD±) 9,253/mm^3 (±4,803.1), ESR was 67 mm/h (±36.7), and CRP level was 72 mg/L (±77.2) in our series. The mean leukocyte count was significantly higher in the PVO than TVO and BVO patients ($P < 0.004$; $P < 0.015$, respectively). ESR and CRP levels were significantly higher in PVO patients when compared with BVO cases ($P < 0.006$; $P < 0.011$, respectively) (Table 6).

Mean diagnostic delay (MDD) in our series was 29.4 weeks. MDD was different according to the etiology

Table 6 Summary of the initial laboratory data

Laboratory data	Pyogenic	Brucella	Tuberculous	Total mean
Leukocytes (/mm^3) mean (range)	11,292 (4,600–31,500)	7,710 (4,800–11,900)	7,559 (4,300–13,000)	9,253
ESR (mm/h) mean (range)	77 (11–140)	46 (4–100)	67 (10–138)	67
C-reactive protein (mg/L, *n*: 0–5) mean (range)	95 (3–398)	34 (3–200)	67 (4–236)	72

(± SD): 422 (±704), 162 (±556.7), and 162 (±282.9) days in TVO, PVO, and BVO, respectively. Statistically no significant differences were present.

Fine-needle aspiration biopsy was performed in 55 (32 pyogenic, 21 tuberculous, and two brucellar) patients by CT-guided method. In the remaining cases, reasons for not performing biopsy were as follows: isolation of the infective agent by blood culture (*n*: 5), previous surgery history suggesting possibility of bacteremia (*n*: 3), previous bacterial infection history where a causative agent was yielded and assumed to be the pathogen responsible for VO (*n*: 2), postoperative spondylodiscitis admitted under nonspecific antibiotherapy (*n*: 1), patient's refusal for biopsy (*n*: 1), TB in an other focus (*n*: 5), previous TB infection (*n*: 3), TB infection in a close relative (*n*: 1), and radiological suspicion of Pott's disease (*n*: 2).

Fine-needle aspiration biopsy culture was performed in all of them, and of these, 24 (44%) were positive. Histopathological examination was done in 40 of them (45 materials had been sent to the pathology unit, but five of them were insufficient for examination), and of these, 30 (75%) were diagnostic. In 84.3% of the PVO patients having had biopsy, the diagnosis was based only on microbiological and/or histopathological examination of the FNAB. FNAB was performed in 21 (66%) of TVO patients. In 90.4% of the patients having had biopsy, the diagnosis was based only on microbiological and/or histopathological examination of the FNAB. Brucellar VO was diagnosed serologically; in two cases, the diagnosis was confirmed by biopsy as well. Death was seen in only one patient.

Discussion

Vertebral osteomyelitis is not a frequent disease; the incidence is 5.3 cases per million per year [10, 11]. But the incidence has been increasing because of growing number of older, immunosuppressive, chronic debilitating diseased patients, and the frequent use of invasive modalities for diagnosis [11, 14]. Intravenous drug use, epidural injections, and spinal instrumentation and surgery are also among the risk factors leading to an increase in the incidence of VO [3, 15]. The diagnosis may be difficult as the symptoms and signs are nonspecific, and the disease has an indolent course [10]. As the treatment of TB is possible, a shift toward pyogenic osteomyelitis is remarkable [15]. PVO is dominant in our series as well.

Men are slightly more frequently affected than women [1, 10]. The disease may affect patients of any age, but advanced age seems to be associated with the highest incidence [15]. In our study also, fifty-nine patients were men. The mean age of the patients was 55 ± 15.6 (SD±) years, and 43% of patients were older than 60 years.

The most common site of infection is the lumbar spine (45–50%), followed by thoracic, cervical, and sacral regions [10]. Lumbar involvement is predominant in our cases (69%) as well. This may be explained by the high percentage (44%) of PVO and the frequent lumbar involvement in our TVO cases.

Spinal pain and paravertebral muscle spasms are the most common clinical findings. Fever may be present in 10–45% of the cases [10, 11]. Other symptoms may include paresthesias, difficulty in motion, anorexia, and malaise. Physical findings may include tenderness on palpation over the involved area, paraspinal spasm, and limitation of motion. Spread of infection into epidural space may result in neurological deficit [10]. In this study, only 49% of patients had fever. All of the patients had suffered from spinal pain, and limited motility was present in 67% of the cases. The high frequency of limited motility of our cases may be due to delay of diagnosis and related to severity of pain. Neurological symptoms such as weakness and numbness were present in 19% of the cases, and the involvement was mostly mild. This may explain why surgery was addressed in only three patients, a low rate as compared with other studies [3].

Mean diagnostic delay is in a wide range in published VO series. It was 2.6 months and 14 weeks in two different series, respectively [11, 16]. In some TVO series, this delay may account up to 6 months [17]. MDD in our series was 29.4 weeks, longer when compared to other studies. In our series, although it was not statistically significant, a relatively longer MDD was observed in TVO patients. Since the signs and symptoms are not specific, this disease may

be easily misdiagnosed as other common disorders of the spine (lumbar discal herniation, low back pain etc.). Additionally, as our center is a tertiary one, most of the cases might have been sent when the initial treatments failed. Also, a more indolent course with a prolonged duration of symptoms up to several months and years may be seen in TVO [15, 18]. In our series, 32% of our patients had TVO, and the diagnosis was established 8 years after the first symptoms in two of them (one of the patient had gibbosity). All these factors may explain the relatively longer duration of diagnostic delay in our patients.

Determination of leukocyte count, CRP levels, and ESR are parts of the first-visit evaluation [15]. Leukocytosis, neutrophilia, and very high values of ESR and CRP may suggest PVO [11]. In TVO, leukocyte level is normal and ESR is high [15]. The mean leukocyte count was significantly higher in the PVO than TVO and BVO patients ($P < 0.004$; $P < 0.015$, respectively). This was seen in some other studies as well [11, 14].

Plain radiography of the spine may localize the lesion, but has been replaced by advanced imaging modalities including CT and MRI [15]. MRI is the most important and most sensitive diagnostic method and permits the differential diagnosis [19]. In our series, MRI was done in 99 patients (one patient was admitted with a CT diagnostic for VO) and was diagnostic in 98% of the patients; only in one patient, MRI findings suggested metastasis. Nine of our patients admitted with a simultaneous CT and MRI, and only in two of them, MRI was superior to CT.

Pyogenic vertebral osteomyelitis

Pyogenic vertebral osteomyelitis was more frequent (44%) in our series, and 23% of these cases had a spinal surgery history due to disk herniation. Similar to other studies, vertebral levels mostly involved were lumbar ones in PVO [3, 11]. In our PVO cases, the rate of fever was 36%. This low rate may be explained by the use of analgesics/antipyretics. We noted that the use of these drugs was reported in our patients with or without fever. The other reason may be the long duration of the disease and use of some antibiotics in a part of the patients. However, even 33% of the patients with positive culture did not have fever. The diagnosis in all cases was established by clinical and radiological findings. Alternative diagnoses including erosive osteochondrosis, metastasis, and noninfectious diseases have been excluded by using those findings.

Spinal infections may cause severe neurological deficit in few cases, but mild involvement is present in 28–35% of the patients [20]. In the review including 51 PVO patients, neurological complications were seen in 33% [21]. Similarly, neurological symptoms were present in nine (20%) of our PVO patients.

Mylona et al. reported that more than one underlying illness was present in PVO cases in their review. One of these 14 studies reviewed by Mylona et al. reported that 28% of patients had no underlying disease [3]. In our series, 16% of patients had no underlying risk factor.

CT-guided FNAB can provide adequate microbiological specimens in 18–86% of cases. This procedure can be repeated if results are negative [22]. In a systematic review, it was reported that biopsy was performed in 79% of the cases (range, 48 to 100%). The reported yield was about 77% (range 47–100%) [3]. Similarly, biopsy was done in 32 (72%) of our patients.

As in many other studies, *S. aureus* was the most frequent isolated microorganism in PVO, followed by aerobic gram-negative bacilli [3, 11, 15, 21, 23, 24]. In 41% of pyogenic infections, a microorganism was isolated. Ten (56%) of these 18 were MSSA.

In patients not suffering from sickle cell disease, *Salmonella* spp. infections accounts for only 0.5% of all osteomyelitis and involvement of the spine is seen in approximately 25% of these cases [25]. In this study, one patient presented with *Salmonella typhi* spondylodiscitis was 75 years old and had chronic lymphocytic leukemia as underlying disease.

Vertebral osteomyelitis due to fungi is rare and either an immunosupression or specific epidemiological exposure history is needed for occurrence [15, 26, 27]. The most common fungal pathogens involved in these infections are *Candida, Aspergillus,* and *Rhizomucor* species. *Blastoschizomyces capitatus (Geotrichum capitatum)* is encountered rarely [28, 29]. In our series, this rare pathogen *G. capitatum* was isolated from a patient having a history of colorectal cancer and chemotherapy.

Excluding the postoperative PVO, source of infection in 23 (52%) of our cases was unknown. This high percentage is similar to the series reported by Pigrau et al. [30]. Likely, in most of the series, either no source is identified or the ratio is low [3].

Recommended duration of therapy ranges from 4 to 6 weeks to 3 months in VO, and parenteral antimicrobial treatment is still the standard modality in VO due to gram-positive bacteria [5]. Outpatient parenteral antimicrobial therapy in outpatient settings may be considered in some cases [31]. If ESR and/or CRP have not normalized, the continuation of therapy per oral should be considered [7]. In our study, 95% of PVO cases were treated medically. After a course of 4–6 weeks of parenteral regimen, the patients were re-evaluated according to clinical (pain, ability to ambulate) and laboratory (leukocyte count, ESR, CRP) parameters. If the response in clinical signs and symptoms (pain, immobility) and in laboratory parameters (ESR, CRP) was suboptimal, treatment was continued up for a one or 2 months per

oral. Only two patients needed abscess drainage, and one had a relapse.

All patients having negative serology for brucellosis, FNAB with negative microbiological results and with a histopathological diagnosis of inflammation suggesting PVO were accepted as probable PVO and treated empirically for 3 weeks as it is hard for patients to accept a second biopsy. If an adequate response was not present in clinical (pain relief) and laboratory parameters, a switch to anti-TB treatment was made. We had 26 such patients, but we did not switch any treatment to TB nor had a progression in these cases. All of them were treated successfully empirically.

Brucellar vertebral osteomyelitis

In Mediterranean countries and in many other areas, brucellosis is an endemic infection [11]. In adults, brucellosis produces VO in 6–12% of cases and VO accounts for 35–50% of all osteoarticular complications [32]. Colmenero et al. reported an incidence of 48% of BVO in 219 cases of VO [11]. Al Soub et al. and Calvo et al. reported an incidence of 21 and 25% of BVO, respectively [33, 34]. In our study also, BVO rate is similarly about 24%, as our country is endemic for brucellosis.

Lumbar and lumbosacral level was involved in 67% of our cases. The reported lumbosacral involvement rate in the series ranges between 68 and 83% [32, 35–37]. Multiple-level involvement was described as 0–9% of cases [35, 37]. Only one of our patients had multiple-level involvement similarly reported by Colmenero et al. [32].

All BVO patients were given doxycycline (200 mg/day) + rifampin (600 mg/day) for 3 months. Neither our patients failed the treatment nor did they need surgery.

Tuberculous vertebral osteomyelitis

In endemic countries, incidence of TB is also high, and it has even increased in the past few years because of HIV. Spinal involvement is one of the most frequent locations of extrapulmonary TB [11]. Thirty-two percent of our cases were diagnosed as TVO.

In cases of TVO, involvement of the thoracic spine is most common [10]. In some of the studies, thoracic vertebral level is predominantly involved [1, 11]. But in others, either the lumbar involvement is more frequent or the lumbar and thoracic involvement rates are equal [38–40]. In our study, the vertebral level involved was thoracic in eight (25%), lumbar in 21 (66%), and sacral and cervico-thoracic in one case. Multiple levels were involved in only one case.

Paraspinal, epidural, and/or paravertebral abscesses were present in 26 (81%) and cord pressure in five (16%) patients. But neurological involvement was present in nine (28%) cases. This low percentage may be explained by the late occurrence of neurological deficit in TVO [15].

All of the patients diagnosed had *Mycobacterium tuberculosis complex* as causative agent except one, *Mycobacterium avium intracellulare complex* (MAC). MAC infections may mimic Pott's disease even in patients who are not immunocompromised; however, the known association with human immunodeficiency virus is observed for spinal infections as well [24]. The interesting feature of our patient was her immunocompetent status.

All TVO patients received anti-TB treatment for 1 year. Three patients (9%) had surgical intervention, and one (3%) had abscess drainage.

In conclusion, our study demonstrated that VO affects mainly patients of advanced age and male gender. The etiological distribution may differ according to geographical areas. Although brucella and TB are endemic in our country, PVO was more frequent. The lumbar vertebral level is mostly involved. Although thoracic involvement may be more predominant in TVO, it is not suggestive of TB in our study. MRI seemed helpful in differential diagnosis of spinal diseases. Microbiological and/or histopathological examinations of CT-guided FNAB are the mainstays for the diagnosis. Suspicion and early diagnosis may decrease the complications.

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