Original Article

Tuberculous, Pyogenic, and Brucellar Vertebral Osteomyelitis: A 10-year Experience

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Abstract

Objective: Spinal osteomyelitis is an uncommon cause of back pain but it has potential to compromise nervous system and even death may occur if it is not treated effectively. We compared the underlying diseases, clinical, and complications among patients with pyogenic (PVO), brucellar (BVO), and tuberculous vertebral osteomyelitis (TVO).

Patients and Methods: In this descriptive-comparative study, all patients older than 1 year who were hospitalized at Rasoul-e-Akram Hospital from 1999 to 2009 with a confirmed diagnosis of VO were included. The diagnosis of VO was confirmed in the presence of compatible clinical features, vertebral CT scan or MRI. Etiological diagnosis of VO was defined when the microorganism was isolated from blood culture, bone biopsy, paravertebral abscess aspiration; typical histopathological pattern of tuberculosis (caseating granuloma) or malignancy in bone biopsy; Wright's or serum agglutination test ≥ 1/80 or 2ME ≥ 1/40 according to the national guidelines. Analytical statistics such as the chi-square and t test were used to find correlation and relationships among the variables. $P< 0.05$ was considered to indicate statistical significance.

Results: A total number of 87 patients studied. There were 62 (71.26%) males and 25 (28.73%) females. Thirty-eight (43.67%) patients had PVO, 26 (29.88%) had TVO, 18 (20.68%) had BVO, 3 (3.4%) had malignant disorder with metastasis to bone, and the remaining 2 (2.29%) cases had fungal VO. Fever and back pain were the most common symptoms in PVO (12), but in TVO the most common symptom was back pain. DM and previous bone spinal surgery were the most common underlying diseases in PVO patients (P=0.000). Paravertebral abscess was reported in 6 (23.7%) patients with TVO and 6 patients (15.78%) with PVO, but no such complication was noted in BVO group.

Conclusion: There are significant differences between VO by different microorganisms that help physician to start empirical medical treatment while waiting to definite diagnosis by blood culture, culture from paravertebral abscess, serology and bone biopsy.

Keywords: Vertebral osteomyelitis; pyogenic osteomyelitis; brucella osteomyelitis; tuberculous osteomyelitis

Introduction

Spinal osteomyelitis is an uncommon cause of back pain but it has potential to compromise nervous system and even death may occur if not treated effectively. The clinical feature of vertebral osteomyelitis (VO) is nonspecific. It starts gradually and follows an indolent course making early diagnosis difficult (1).

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The incidence of vertebral osteomyelitis with Staphylococcus aureus is sharply increasing (2), but its diagnosis is difficult because of vague and diffuse symptoms and signs on presentation, and the fact that clinical data might be obscured by the symptoms of underlying diseases (3).

Brucellosis remains a noticeable public health in the Middle East.The most common etiologic agent in Iran is B. melitensis (4). Hasanjaniroushan and his colleagues reported that 32 out of 469 patients with brucellosis suffered from spondylitis (5). Brucella vertebral osteomyelitis (BVO) may be complicated by neurological defects that must be considered in endemic areas (6).

Tuberculous vertebral osteomyelitis (TVO) is common in the both developed and developing countries. Familiarity with clinical manifestations of TVO is crucial to diagnose this condition. In contrast to pyogenic vertebral osteomyelitis (PVO) that the pain is usually severe in the early stages of the disease, the progress of pain in TVO is gradually and becomes severe in later stages (7).

The aim of this study was to describe the clinical features, laboratory data and complications of patients with VO,

with attention to the differential aspects of TVO, PVO, and BVO, admitted to the Rasoul-e-Akram Hospital during 10 years.

Patients and Methods

In this descriptive-comparative study, all patients older than 1 year who were hospitalized in Rasoul-e-Akram Hospital between 1999 and 2009 with a confirmed diagnosis of VO were included. The diagnosis of VO was confirmed in the presence of compatible clinical features (fever and spinal pain with inflammatory features) and imaging studies (irregular erosions in the end plates of adjacent vertebral bodies, narrowing of the intervening disk space, and epidural, paraspinal or psoas abscess). Vertebral CT scan or MRI was done for all patients.

Etiological diagnosis of VO was defined when the microorganism was isolated from blood culture, bone biopsy, or paravertebral abscess aspiration; typical histopathological pattern of tuberculosis (i.e., caseating granuloma) or malignancy was observed in bone biopsy; Wright's or serum agglutination test ≥ 1/80 or 2ME ≥ 1/40 according to national guidelines (8).

All demographic data, clinical manifestations, underlying disease, laboratory findings (CBC, ESR, CRP, culture results, pathology, and serology), Tuberculin Skin Test (TST), surgery and other necessary data were recorded in special data sheets.

WBC≥ 12000/µl, ESR> 17mm/hr for men and > 25mm/hr for women and CRP≥ 12mg/l, TST≥ 10 mm were considered as the cut-off levels.

After that, all the data were brought out from the data sheets and analyzed by the statistical software SPSS 15. Descriptive statistics of frequency, central tendency indices consisting of mean, and dispersion indicator consisting standard deviation were used to evaluate the results. Analytical statistics such as the chi-square and t test were used to find correlation and relationships among the variable. P< 0.05 was considered to indicate statistical significance.

This study was approved by the Research Deputy of Tehran University of Medical Sciences, Faculty of Medicine (Pardis Hemmat).

Results

During the study period, a total number of 114 patients had been diagnosed as having VO in Rasoul-e-akram Hospital but only 87 cases had confirmed diagnosis. Of this, 62 (71.26%) patients were male and 25 (28.73%) patients were female. Mean age of the patients was 44.8 years (range, 5-76 years).

Thirty-eight cases (43.67%) had PVO, 26 (29.88%) had TVO, 18 (20.68%) had BVO, 3 (3.4%) had malignant disorder with metastasis to bone, and the remaining 2 cases (2.29%) had fungal VO (FVO, candida albicans diagnosed by culture).

Clinical manifestations and laboratory data are shown in Tables 1 and 2, respectively.

Table 1. Frequency (percentage) of clinical manifestations in patients with vertebral osteomyelitis (VO)

Symptoms and sign	Pyogenic VO (N = 38)	Tuberculous VO (N= 26)	Brucella VO (N= 18)	P value
Fever	34 (89.4%)	6 (23%)*	14 (77.7%)	0.003
Pain	38 (100%)	26 (100%)	16 (88.8%)	NS1
Neurological symptoms (paresthesias, paralysis)	10 (26.31%)	16 (61.53%)*	6 (33.3%)	0.001

*significant difference with respect to the other groups.
1. NS= non-significant (among PVO, TVO, and BVO)

Table 2. Laboratory data in patients with VO

Lab. Data	Pyogenic VO	Tuberculous VO	Brucella VO	P value
Elevated ESR	34 (89.4%)	20 (76.9%)	8 (44.4%)*	0.002
Elevated CRP	28 (73.6%)	20 (76.9%)	16 (88.8%)	NS
Leukocytosis	14 (36.8%)	0[1]	6 (33.3%)	0.000
Positive TST	0	8 (30.7%)[1]	0	0.000
Bone biopsy [2]	8 (21%)	26 (100%)	0*	0.000

*Significant difference with respect to the BVO
1. Significant difference with respect to the TVO
2. Bone biopsy was done in 34 patients

Paravertebral abscess was reported in 6 (23.7%) patients with TVO and 6 (15.78%) patients with PVO (P= 0.000 with respect to BVO). We do not have P value of 0 in biostatistics, please correct it. If the number is very small, you may use P< 0.001.

The sentence should be rewritten. How many paravertebral abscesses were recorded in brucella patients?

In patients with TVO, 2 patients (7.6%) had positive smear for acid-fast bacilli (AFB) in bone biopsy specimen and the other had pathologic finding consistent with tuberculosis.

DM and previous bone spinal surgery were the most common underlying diseases in PVO patients (P= 0.001). The mean duration of symptoms before diagnosis is shown in Table 3.

Table3. The mean duration of symptoms before diagnosis in VO.

	Less than 3 months	3-6 months	More than 6 months	P value
PVO	28 (73.6%) *	6 (15.7%)	4 (10.5%)	0.002
TVO	4 (15.3%)	10 (38.4%)	12(46.3%) *	0.001
BVO	10 (55.5%)	8 (44.5%)	0*	0.000

*significant difference with respect to the other groups

Blood culture was performed in all cases. It was negative in all patients with TVO and BVO. However, blood culture was positive in 26 cases of PVO, *S. aureus* in 20 cases and gram negative bacilli (E. coli and Klebsiella spp.) in 6 cases. *S. aureus* was isolated in paravertebral abscess material in 8 cases who underwent surgery, but blood culture was negative in 4 cases.
Eight patients (30.7%) with TVO and 10 patients (26.3%) with PVO underwent surgery because of paravertebral abscess and pathologic fracture, but all BVO patients were treated by medical therapy (P= 0.001) .

In BVO group 14 patients and in TVO group 20 cases were followed for one year. All of them were symptom-free. Unfortunately patients with PVO were not followed.

Discussion

Vertebral osteomyelitis is an uncommon infection. However, its incidence is increasing owing to frequent use of invasive procedures, spinal surgery, and growing number of immunosuppresed patients and people with debilitating diseases (9, 10).
We found that most patients suffered from PVO and in consistent with other studies, *S. aureus* was the most frequent isolated organism in this group followed by gram negative bacilli (11, 12).
We confirmed that underlying diseases have discriminative role to diagnose PVO from TVO and BVO. The association of some underlying diseases such as diabetes mellitus (DM), injection drug use and surgery with PVO has been reported. Colmenero et al. found that previous focal infection and/or bacteremia, DM, and bone spinal surgery were the most common risk factors in patients with PVO, respectively (11). Allan et al. reported that vascular disease, immunosuppressive therapy, and DM were the most predisposing factors in patients with PVO (3).
In compatible to other studies we found that fever and back pain were the most common symptoms in PVO (13), but in TVO the most common symptom was back pain, so TVO should be considered in the differential diagnosis of patients with chronic back pain (14).
In consistent with Colmenero study, the absence of fever, neurological symptoms, and paravertebral and epidural abscess were significantly more frequent in TVO in comparison to two others groups (11). Delaying in diagnosis may explain the high frequency of complication in this group because a clear relation exists between delayed diagnosis and the presence of more destructive lesions and neurologic deficits (15, 16).
Sacroiliitis and spondylitis are the most frequent clinical forms of osteoarticular involvement in patients with brucellosis. Hassanjaniroushan reported that 32 cases out of 469 patients (6.82%) with brucellosis suffered from spondylitis (5). Colmenero et al. showed that the incidence of VO among 918 patients with brucellosis was 10.4% (17).
Brucellar epidural abscess is very rare (18) and we did not find any complication in patients with BVO. In contrast to the current finding and other studies (18-20), Colmenero showed that 10% of patients with BVO had psoas abscess (17).
Inflammatory markers such as ESR and CRP are sensitive, but lack the specificity required to be clinically useful in ruling out PVO (21). We found that increased ESR and leukocytosis were more frequent in PVO, in fact, when leukocytosis, increased ESR and CRP are present, these findings are suggestive of PVO (16, 22). In comparison to Weng study, our TVO patients had elevated ESR, and CRP serum levels without leukocytosis (14). In our study patients with BVO had more frequent elevated CRP levels in comparison to other groups. Colmenero reported that 75% of patients with BVO had elevated serum CRP levels (17).
In our study, only eight patients in TVO group had positive TST and PPD was less than 10 mm in patients with BVO and PVO. Similar to Bowerman study we concluded that a positive TST (≥ 10 mm) was associated with TB infection, and high BCG vaccination coverage does not appear to limit the usefulness of the TST as a tool for diagnosing TB (23).
Etiologic diagnosis of VO is difficult, requiring in 93.2% of cases the performance of bone biopsies (11). The success rate of CT-guided bone biopsy for identification of etiologic agent in VO is 76-91% (24). In our study nearly 50 percent of patients needed bone biopsy to make the diagnosis. Bone biopsy was necessary to establish the diagnosis in 100% of TVO and 21% of PVO, because of high diagnostic yield of standard agglutination test for brucellosis, bone biopsy was not done for any patient in this group.
Colmenero showed that 45% of patients with VO underwent surgical intervention for therapeutic purposes (11), but in our study only in 20.68% of the patients, surgical intervention was performed to treat the osteomyelitis. Since surgical intervention is generally

indicated in cases who develop complications, the lower rate of surgical intervention here compared to Colmenero study may be related to less prevalence of complications such as paravertebral abscess or neurologic deficits in our series.

In conclusion, we showed that there are significant differences between TVO, BVO, and PVO according to clinical and laboratory findings. These differences help physicians to after obtaining blood culture, bone biopsy, paravertebral abscess culture, serology, and other useful diagnostic tests.

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References

1. Eismont FJ, Bohlman HH, Soni PL, Goldberg VM, Freehafer AA. Pyogenic and fungal vertebral osteomyelitis with paralysis. J Bone Joint Surg Am 1983; 65(1): 19-29.
2. Espersen F, Frimodt-Moller N, Rosdahl VT, Skinhoj P, Bentzon MW. Changing pattern of bone and joint infections due to staphylococcus aureus: study of cases of bacteremia in Denmark, 1959-1988. Rev Infect Dis 1991; 13(3): 347-358.
3. Jensen AG, Espersen F, Skinhoj P, Frimodt-Moller N, Bacteremic staphylococcus aureus spondylitis. Arch Intern Med 1998; 15(9): 509-18.
4. Makarem EH, Karjoo R, Omidi A. Frequency of brucella melitensis in south Iran. J Trop Pediatr 1982; 28(2): 97-100.
5. Hassanjani Roushan MR, Mohrez M, Smailnejad Gangi SM, Soleimani Amiri MJ, Hajiahmadi M. Epidemiological features and clinical manifestations in 469 adult patients with brucellosis in Babol, Northern Iran. Epidemiol Infect 2004; 132(6): 109-14.
6. Mousa AM, Bahar RH, Araj GF, Koshy TS, Muhtaseb SA, Al-Mudallal DS, et al. Neurological complications of brucella spondylitis. Acta Neurol Scand 1990; 81(1): 16-23.
7. Wang D. Diagnosis of tuberculosis vertebral osteomyelitis (TVO) in a developed country and literature review. Spinal cord 2005; 43(9): 531-42.
8. Center for Disease Control, office of the Deputy for Public Health, Ministry of Health and Medical Education of the I.R. Iran. National guideline against Brucellosis. Tehran 2007. In Persian.
9. Torda AJ, Gottlieb T, Bradbury R. Pyogenic vertebral osteomyelitis: analysis of 20 cases and review. Clin Infect Dis 1995; 20(2): 320-8.
1. Cahill DW, Love LC, Rechtine GR. Pyogenic osteomyelitis of the spine in the elderly. J Neurosurg 1991; 74(6): 878-86.
2. Colmenero JD, Jimenez-Mejias ME, Sanchez-Lora FJ, Reguera JM, Palomino-Nicas J, Martos F, et al. Pyogenic, tuberculous, and brucellar vertebral osteomyelitis: a descriptive and comparative study of 219 cases. Ann Rheum Dis 1997; 56(12): 709-15.
3. Perronne C, Saba J, Behloul Z, Salmon-ceron D, Leport C, Vilde JL, et al. Pyogenic and tuberculous spondylodiscitis(vertebral osteomyelitis) in 80 adult patients. Clin Infect Dis 1994; 19(4): 746-50.
4. Mylona E, Samarkos M, Kakalou E, Fanourgiakis P, Skoutelis A. Pyogenic vertebral osteomyelitis: a systemic review of clinical characteristics. Semin Arthritis Rheum 2009; 39(1): 10-17.
5. Weng CY, Chi CY, Shih PJ, Ho CM, Lin PC, Chou CH, et al. Spinal tuberculosis in non-HIV infected patients: 10 year experience of a medical center in central Taiwan. J Microbiol Immunol Infect 2010; 43(6): 464-9.
6. Janssens JP, De Haller R. Spinal tuberculosis in a developed country. A review of 26 cases with special emphasis of abscesses and neurologic complications. Clin Orthop 1990; 257: 67-75.
7. Kim CJ, Song KH, Jeon JH, Park WB, Park SW, Kim HB, et al. A comparative study of pyogenic and tuberculous spondylodiscitis. Spine (Phila pa 1976). 2010; 35(21): E 1096-100.
8. Colmenero JD, Ruiz-Mesa JD, Plata A, Bermudez P, Martin-Rico P, Queipo-Ortuno MI, et al. Clinical findings, therapeutic approach, and outcome of brucellar vertebral osteomyelitis. Clin Infect Dis 2008; 46(3): 426-33.
9. Ates O, Cayli SR, Kocak A, Kutlu R, Onal RE, Tekiner A. Spinal epidural abscess caused by brucellosis. Two case reports. Neurol Med Chir(Tokyo) 2005; 45(1): 66-70.
10. Turunc T, Turunc T, Demiroglu YZ, Colakoglu S. Retrospective evaluation of 15 cases with psoas abscess. Mikrobiyol Bul 2009; 43(1): 121-5.
11. Sharif HS, Aideyan OA, Clark DC, Madkour MM, Aabed MY, Mattsson TA, et al. Brucellar and tuberculous spondylitis: Comparative imaging features. Radiology 1989; 171(2): 419-25.
12. An HS, Seldomridge JA. Spinal infections: diagnostic tests and imaging studies. Clin Orthop Relat Res 2006; 444: 27-33.
13. Buchelt M, Lack W, Kutschera HP, Katterchafka T,Kiss H, Schneider B, et al. Comparison of tuberculous and pyogenic spondylitis. An analysis of 122 cases. Clin Orthop 1993; 296: 192-9.
14. Bowerman RJ. Tuberculin skin testing in BCG-vaccinated populations of adults and children at high risk for Tuberculosis in Taiwan. Int J Tuberc Lung Dis 2004; 8(10): 1228-33.
15. Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant –related staphylococcal infections: a randomized controlled trial. JAMA 1998; 279: 1537-41.