ORIGINAL ARTICLE 10.1111/1469-0691.12653

Vertebral osteomyelitis: clinical features and diagnosis

Ş. Eren Gök[1], E. Kaptanoğlu[2], A. Çelikbaş[1], Ö. Ergönül[3], N. Baykam[1], M. Eroğlu[1] and B. Dokuzoğuz[1]

1) *Infectious Diseases and Clinical Microbiology Clinic, Ankara Numune Training and Research Hospital, Ankara,* 2) *School of Medicine, Neurosurgery Department, Neareast University, Cyprus, and* 3) *School of Medicine, Infectious Diseases and Clinical Microbiology Department, Koç University, Istanbul, Turkey*

Abstract

We aimed to describe clinical and diagnostic features of vertebral osteomyelitis for differential diagnosis and treatment. This is a prospective observational study performed between 2002 and 2012 in Ankara Numune Education and Research Hospital in Ankara, Turkey. All the patients with vertebral osteomyelitis were followed for from 6 months to 3 years. In total, 214 patients were included in the study, 113 out of 214 (53%) were female. Out of 214 patients, 96 (45%) had brucellar vertebral osteomyelitis (BVO), 63 (29%) had tuberculous vertebral osteomyelitis (TVO), and 55 (26%) had pyogenic vertebral osteomyelitis (PVO). Mean number of days between onset of symptoms and establishment of diagnosis was greater with the patients with TVO (266 days) than BVO (115 days) or PVO (151 days, $p < 0.001$). In blood cultures, *Brucella* spp. were isolated from 35 of 96 BVO patients (35%). Among 55 PVO patients, the aetiological agent was isolated in 11 (20%) patients. For tuberculin skin test >15 mm, sensitivity was 0.66, specificity was 0.97, positive predictive value was 0.89, negative predictive value was 0.88, and receiver operating characteristics area was 0.8. Tuberculous and brucellar vertebral osteomyelitis remained the leading causes of vertebral osteomyelitis with delayed diagnosis. In differential diagnosis of vertebral osteomyelitis, consumption of unpasteurized cheese, dealing with husbandry, sweating, arthralgia, hepatomegaly, elevated alanine transaminase, and lumbar involvement in magnetic resonance imaging were found to be predictors of BVO, thoracic involvement in magnetic resonance imaging and tuberculin skin test > 15 mm were found to be predictors of TVO, and history of spinal surgery and leucocytosis were found to be predictors of PVO.

Keywords: *Brucella*, pyogenic, tuberculosis, vertebral osteomyelitis
Original Submission: 23 November 2013; **Revised Submission:** 11 April 2014; **Accepted:** 23 April 2014
Editor: D. Raoult
Article published online: 28 April 2014
Clin Microbiol Infect

Corresponding author: O. Ergonul, Koç University, School of Medicine, Infectious Diseases and Clinical Microbiology Department, Rumelifeneri, Sariyer, Istanbul 34450, Turkey
E-mail: oergonul@ku.edu.tr

Introduction

Vertebral osteomyelitis (VO) is a compelling clinical entity for clinicians, because of its insidious start and indolent course, which make diagnosis difficult. As a consequence, patients often develop destructive lesions or neurological complications related to compression of the spinal cord or its roots [1]. Vertebral osteomyelitis is an infrequent infection; however, the incidence is increasing because of the growing number of older patients and chronic diseases [1]. In many reports VO was grouped as brucellar (BVO), tuberculous (TVO) and pyogenic (PVO) [1,2]. Some studies reported only one clinical entity [3]; however, comparable studies are necessary for differential diagnosis of these disease entities for management of patients.

Diagnostic studies of VO differ according to the prevalence of these diseases. This study was performed in Turkey, where brucellosis and tuberculosis are more common than in European and North American countries. By this prospective study, we aimed to describe clinical and diagnostic features of VO for differential diagnosis and treatment.

Materials and Methods

This is a prospective observational study performed between 2002 and 2012 in Ankara Numune Education and Research Hospital in Ankara, Turkey. Diagnosis of VO was made

according to clinical, radiological and microbiological criteria, which were defined previously [4,5]. The diagnostic algorithm was performed according to (i) clinical symptoms suggestive of VO, (ii) laboratory abnormalities—complete white blood cell count, erythrocyte sedimentation rate, C-reactive protein level, Brucella tube agglutination test of serum and/or cerebrospinal fluid, tuberculin skin test (TST), (iii) abnormal magnetic resonance imaging (MRI) or computed tomography scan features compatible with infection of the spine, (iv) isolation of the causative microorganism, typical histological pattern from percutaneous disc or epidural abscess puncture or biopsy, and specific tests for microorganisms.

Patients were included if there was illness compatible with vertebral infection and evidence of spinal involvement from imaging. Definite diagnosis of TVO was considered when *Mycobacterium tuberculosis* was isolated from a sample of vertebral, paravertebral or epidural tissue or from a psoas abscess. Probable TVO diagnosis was considered when caseating granulomas, with or without acid-fast bacilli, PCR positivity in a vertebral biopsy and TST positivity were found, or when *M. tuberculosis* was isolated from another focus of infection such as sputum, urine and cerebrospinal fluid. Presumptive diagnosis of TVO was considered when positive findings by imaging, plus positive TST, and no response to non-specific antibiotics but response to anti-tuberculosis treatment were reported. Definite BVO was considered when *Brucella* spp. were isolated from a sample of vertebral, paravertebral or epidural tissue or from a psoas abscess, from blood or other body fluid or tissue specimens, or when *Brucella* standard tube agglutination of >1/160 was found in addition to clinical findings compatible with VO. Definite PVO was considered when a microorganism was isolated from the involved vertebra, intervertebral disc space, or paravertebral or epidural abscesses. Probable PVO was considered when the results of at least two blood cultures were positive during a compatible illness. Presumptive PVO was considered when an organism was isolated from urine, stool and wound, if a sinus tract was detected in contiguity with the vertebral lesions, if there was a history of vertebral surgery, and if empiric antibiotic therapy was successful. For each disease entity, the other two entities were ruled out. All the patients with VO were followed for from 6 months to 3 years. Informed consent was obtained from patients.

Statistical analysis

Chi-square test was used for comparison of categorical variables and *t*-test was used for comparison of continuous variables. Multivariate analysis was performed for detection of the predictors of each disease category separately. Independent variables were selected from the statistically significant variables listed in Tables 1 and 2. In multivariate analysis for the predictors of BVO, consumption of unpasteurized cheese, dealing with husbandry, sweating, arthralgia, hepatomegaly, elevated alanine transaminase, and lumbar involvement in MRI were included in the regression model. In multivariate analysis for prediction of TVO, thoracic involvement in MRI and TST >15 mm were included in the regression model. In multivariate analysis for prediction of PVO, history of spinal surgery and leucocytosis were included in the model. A backward selection process was run. In analysis, STATA version 11 (StatCorp, College Station, TX, USA) was used, and statistical significance was set as $p < 0.005$.

Results

In total, 214 patients were included in the study, 113 (53%) were female. Out of 214 patients, 96 (45%) had BVO, 63 (29%) had TVO and 55 (26%) had PVO. The mean age of the patients with TVO was lower than that of the patients with BVO and PVO (43 versus 53 and 53 years, $p < 0.001$, Table 1). Consumption of fresh cheese and dealing with husbandry, and being a farmer were more commonly reported among the patients with BVO ($p < 0.001$, Table 1). Diabetes mellitus was more common among patients with PVO (33%) than patients with BVO (15%) or TVO (33%, p 0.028, Table 1). The history of spinal surgery was more common among the patients with PVO (64%) than the patients with BVO (11%) or TVO (13%, $p < 0.001$, Table 1).

Fever as a symptom or sign was not statistically different among the three groups; however, sweating was more common (81%) among the patients with BVO ($p < 0.001$, Table 1). The history of upper back pain and cervical pain were more common in patients with TVO (p 0.016 and p 0.014, respectively) than in those with BVO and PVO. However, leg pain was more common among patients with PVO (p 0.003, Table 1). Urinary and defecation incontinence were reported in two patients with PVO and one patient with BVO. Haemoptysis was reported in one of the patients with TVO. Among 96 patients with BVO, 23 (24%) were diagnosed as having neurobrucellosis.

Among TVO cases, 25% had definite diagnosis, 21% probable diagnosis, and so 46% had definite or probable diagnosis. Among BVO cases, all were considered to be definite diagnoses, whereas among PVO cases, 58% were diagnosed as definite or probable (Table 3). Distribution of bacterial agents were, six methicillin-sensitive *Staphylococcus aureus*, one methicillin-resistant *S. aureus*, two methicillin-resistant coagulase-negative *S. aureus* and two *Escherichia coli*. In urinary culture, a total of 11 aetiological agents were isolated, one *Salmonella* Virchow, seven *E. coli*, (four