Vertebral Osteomyelitis; Methods for Diagnosis and Means of Treatment

Jamal Wadi MD, Ayman Raweh MD*, Osama Abu Atta MD**, Obadah Horany MD**, Sufian Rifa'ei MD**, Abdullah Al-Quadan MD^, Basel Jaber MD^*

ABSTRACT

Objective: Vertebral osteomyelitis is an uncommon illness; adults are mostly affected. Our objective is to evaluate the short term outcome of oral versus parenteral antimicrobials treatment for pyogenic (non-tuberculous and non-brucellosis) vertebral osteomyelitis, and the best invasive diagnostic method yielding a microbiological diagnosis.

Methods: The medical records were reviewed in a retrospective study for patients ≥ 18 years old from five urban hospitals within Amman-Jordan; two teaching and three primary care hospitals, during the period between August 1999 to June 2007. Due to the small numbers in the arm of antimicrobials treatment, t-students' test was used to assess inferences like 95% confidence interval and p-values for the difference among treatment arms.

Results: Seventy-four medical records were available, inpatients records 35 from two teaching hospitals, 39 records from three primary care hospitals. The orally treated patients showed lack of difference against the parenteral therapy group at the end of 6 weeks therapy ($p > 0.05$). Diagnostic methods tested for microbiological diagnosis were as follows; True cut biopsy, fine needle aspiration and limited laminectomy did not differ significantly in their microbiological diagnostic ability. Our data suggested lack of difference between oral and parenteral therapy groups at the end of six weeks treatment, but a questionable tendency (95% CI; -0.11 to 0.64, $p= 0.08$). The diagnostic ability of the three methods did not suggest significant differences ($p >0.05$), except for true cut biopsy versus fine needle aspiration where it showed tendency (95% CI; - 0.20 to 0.42, $p= 0.07$).

Conclusion: The key to successful management is the early diagnosis, and bone sampling for microbiological examination, allowing proper antimicrobial selection. A proper bone sampling method is important to evaluate, especially in the absence of surgical indication and the co-notation in some parts of the world that M. tuberculosis is the most -if not the sole- pathogen in vertebral osteomyelitis.

Key words: Oral treatment, Vertebral osteomyelitis, Vertebral osteomyelitis diagnostic procedure.

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Introduction

Vertebral osteomyelitis (VO) is an uncommon disease, with incidence ranges between 1-7% of bone infections, and occurs at a rate of 1/100,000 in the general population, its incidence is increased in the immunocompromised and with the increased

From the Departments Infectious Diseases:
*Jordan Hospital and Medical Center, Amman-Jordan
**The Islamic Hospital, Amman-Jordan ^ Al Khalidi Medical Center, Amman-Jordan
Correspondences should be addressed to Dr. J. Wadi, Office 11, 3rd floor, Jordan Hospital & Medical Center
P. O. Box 143589 Amman 11814 Jordan, E-mail: Jamalwadimd@yahoo.com
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number of invasive procedures as part of diagnostic and therapeutic interventions. Before the advent of antibiotics large proportions of patients with spinal infections died, estimated to be 40-70%.[1-3] Well controlled studies addressing different aspects of VO have been sparse like best diagnostic method(s), empiric antimicrobials treatment regimen whether parenteral or oral, and the best empiric antimicrobial regimen used in the absence of cultivable organism, especially in the era of availability of modern antimicrobial agents with descent bone penetration like linezolid and tigecycline.[4-9] Some oral agents are useful in the suppressive phase of VO treatment however; oral antimicrobial agents are not widely recommended in the initial phase of VO treatment.

The short-term outcome of treatment was not addressed in earlier studies; somewhat long-term outcome and mortality were evaluated. In addition, case reports based on microorganisms reporting are abundant, whether common microorganisms in endemic areas like in Brucellosis and Salmonellosis, or rare ones like in, Aspergillus, Candida, Rhodococcus and Bartonella henselae.[1,10-17]

Some studies showed that S. aureus, Coagulase Negative Staphylococcus (CoNS) and gram-negative bacilli were dominating.[3,10,11,18]

This study was conducted to evaluate the short term outcome of oral versus parenteral antimicrobials treatment for pyogenic (non-tuberculous and non-brucellosis) vertebral osteomyelitis, and the best invasive diagnostic method yielding a microbiological diagnosis.

Methods

Study design, setting and inclusion criteria:

This is a retrospective study from five hospitals; two teaching, each of about 320 beds and three urban primary care hospitals, each of about 100-120 beds. Approval for the study by the medical administrators and/or ethics committee was obtained for the teaching hospitals. Patients' records were reviewed utilizing the following search terms; vertebral osteomyelitis, unspecified osteomyelitis and disciitis for the period between August 1999 and June 2007. Patients were considered for analysis if they were 18 years old or older and finished six weeks of therapy, and they received antimicrobials as parenteral, oral or combined therapies (two weeks of parenteral therapy followed by four or more weeks of oral therapy). Postoperative VO patients were also included. Excluded patients were eight; younger than eighteen years were 4, fractures 2, one with a tumor and one diagnosed as degenerative disease (Table1).

Statistical analysis:

SPSS software version 15 was used. Study variables were analyzed like the short-term outcome of oral versus parenteral antimicrobials, and best invasive diagnostic method yielding a microbiological diagnosis. Due to the small numbers in the arm of antimicrobials treatment, t-students' test was used to assess inferences like 95% confidence interval and p-values for the difference among treatment arms.

Results

Patients Demographic Features:

Eighty-two patients were available for review; eight patients were excluded (Table I). Seventy-four patients met the diagnosis of VO inpatients were 35. Thirty-nine (52.7%) patients were from other three primary care hospitals. Postoperative VO was found in 9 (12.1%) cases, four (5.4%) patients with paravertebral abscesses, two of which were tuberculous. There were 74 patients with 74 episodes of VO, the mean age was 49.5 years (males mean age was 50.9 years, females mean age was 46.9 years). Males made up 48 (64.9%) and females 26 (35.1%). Fifty (72.4%) patients had no comorbidities and in the rest, diabetes mellitus was the most common comorbidity. Data for the site and extent of disease were available for 69 patients, the lumbar vertebrae were mostly affected; lumbar 42 (60.8%), lumbosacral 10 (14.5%), and 22 (29.7%) other sites. The majority of patients, 61 (88.4%) got more than one vertebra involved; two adjacent vertebrae in 46 (69.7%), three adjacent vertebrae in 9 (13.6%) (Table II).

Diagnostic procedures:

Eighty-one diagnostic procedures were available for 62 patients. In twelve patients the information was not clear which procedure(s) gave the diagnosis and were excluded (Table III). True cut biopsy (TCB) was done in 42 patients with positive microbiological result in 24 (57%), fine needle aspiration (FNA) in 13 patients with positive microbiological result in 6 (46%), laminectomy (LL) in 26 with positive microbiological result in14 (54%). The paired comparisons between the three diagnostic groups in getting a microbiological diagnosis showed lack of means' difference between

Table I. Patients flow and distribution

Total number of patients	82
Total number of excluded patients	8
Younger than 18 yrs of age	4
Diagnosed as a fracture	2
Diagnosed as a tumor	1
Diagnosed as degenerative disease	1
Total number of studied patients	74 (100%)
Post operative cases	9 (12.1%)
Patients with abscess	4 (5.4%)
Patients from three primary care hospitals*	39 (52.7%)
Patients from the two teaching hospitals	35 (47.3%)

* Including patients from Al Khalidi Medical Center, the Specialty Hospital and the Arab Medical Center

Table II. Demographic characteristics and clinical features of 74 cases of Vertebral Osteomyelitis

Feature	**Number of patients/ Total numbers available for analysis**	
Age	Mean ± SD	49.5 ± 14.0 yrs
	Range	22-76 yrs
Gender	Male	48/74 (64.9%)
	Female	26/74 (35.1%)
Residence	Jordanians	36/74 (48.6%)
	Other Arabs	36/74 (48.6%)
	Not entered	2/74(2.7%)
Anatomical location	Lumber	42/69 (60.9%)
	Lumbosacral	10/69 (14.5%)
	Thoracic	8/69 (11.6%)
	Cervical	4/69 (5.8%)
	Thoracolumbar	3/69 (4.3%)
	Sacral	1/69 (1.4%)
	Cervicothoracic	1/69 (1.4%)
Extent of Disease	One vertebra	8/69 (11.6%)
	Two vertebrae or more	61/69 (88.4%)
Morbidities	Diabetes mellitus	18/69 (26.5%)
	Renal failure	2/69 (2.7%)
	Bone and joint diseases	1/69 (1.4%)
	No Comorbidity	50/69 (72%)
	Not available	5/69 (7.2%)

Table III. Eighty one Invasive procedures used in the diagnosis of available 62 patients with Vertebral Osteomyelitis

Finding	Positive finding/total number of available invasive procedures
True Cut Biopsy	24/42 (57%)
Fine needle aspiration	6/13 (46%)
Limited laminectomy	14/26 (54%)
Procedure-recovered microbiological findings for 44 patients in whom data were available	
S. aureus (including 5 MRSA*)	8/44 (22.7%)
CoNS**	5/44 (11.3%)
Brucellosis	4/44 (9.0%)
Tuberculosis	10/44 (22.7%)
Salmonellosis	1/44 (2.2%)
Other includes (Burkholderia cepacia, Proteus mirabilis, 2 pseudomonas, E. coli, Serratia, Acinetobacter, Klebsiella, one case from above (Klebsiella plus MRSA).	8/44 (18.1%)
No growth	17/44(38.6%)

*MRSA = Methicillin-resistant Staphylococcus aureus **CoNS = Coagulase Negative Staphylococcus

procedures; TCB vs. LL (95%CI; -0.23 to 0.29, p = 0.4). TCB vs. FNA (95%CI; - 0.20 to 0.42, p= 0.07). FNA vs. LL (95%CI; -0.25 to 0.41, p=0.3).

Forty-four patients in whom data were available (Table III): Eight (18%) isolates were Staphylococcus aureus (six MRSA, one case postoperative). Five (11.3%) isolates were CoNS, none recorded to have previous hardware in his/her back. Mycobacterium tuberculosis constituted 10 (22.7%) isolates. Brucellosis constituted 4 (9.0%) plus two from blood culture. (Patients with tuberculosis and brucellosis were excluded from treatment analysis). One case (2.2%) was Salmonellosis. The rest of the microbiological isolates were 8 (18.1%) different gram negative bacilli, and the remaining 17(38.6%) showed no growth.

Antimicrobials therapies follow up:

Fifty-three patients were available at the end of six weeks of therapy for follow up; forty one (77.3%) of the followed up patients had improvement in pain and ambulation. Parenteral therapy constituted only 9 patients, four (44.4%) patients showed improvement in pain and ambulation. Combined therapies were administered in 21 patients, ten (47.6%) showed improvement of pain and ambulation, when compared with parenteral therapy there was no significant difference (95% CI; - 0.32 to 0.35, p = 0.4). The oral therapy group, our main concern to analyze, excluding MTB and brucellosis-constituted 24 patients: seventeen (70.8%) patients showed improvement in pain and ambulation, when compared with parenteral therapy (95% CI; -0.11 to 0.64, p = 0.08). Anti-tuberculosis therapies were used in 10 patients, anti-brucellosis regimen in 6 patients (two were diagnosed by blood cultures), both groups were excluded from analysis.

Radiological diagnosis:

Imaging data were available for 72 patients. MRI was utilized in 65 patients from whom 61 (93.8%) patients findings were described as diagnostic of VO, CT scan data were available for 15 patients from whom 8 (53.3%) patients' findings were diagnostic of VO.

Erythrocyte Sedimentation Rate:

Seventeen paired orally treated patients were available for analysis. The ESR improvement in means difference for the oral showed significant improvement (means' difference: 95% CI 11.5–52.3, p= .004), likewise the combined therapy group improvement at the start and at the end of six weeks therapy were (95% CI 9.2–52.4, p = 0.009), and likewise the parenteral treatment group with significant means difference i.e. improvement (95% CI 7.4-71, p = 0.02).

Discussion

The primary outcome measures were to evaluate the short term outcome benefit at the end of 6 weeks for the oral therapy group (excluding tuberculosis and brucellosis, since both infections' treatment is essentially oral), and the ability of the three tested invasive diagnostic procedures in obtaining a microbiological diagnosis. We compared the outcome of the three arms of treatment in pairs, the oral, the parenteral, and combined at the end of six weeks therapy. This comparison was made to identify if we can formulate some different treatment recommendation about the method of antimicrobial administration i.e. employing the oral therapy and whether it is as good as the parenteral therapy, as our review did not materialize studies based on oral therapy.[1,3,10] The oral therapy group did not suggest a significant difference from parenteral therapy for improvement, but rather tendency (95% CI; -0.11 - 0.64, p= 0.08). The combined therapy group and the parenteral group did not show a significant difference though it is marginal (95%CI; -0.048 - 0.512, p= 0.055). The availability of oral antimicrobial agents with proper spectrum, high bioavailability and good bone concentration may argue to employ them, at least in some patients suffering from microorganisms that respond to those oral regimens, prospective randomized studies are needed with this regard.

TCB is a reliable and practical procedure for obtaining a microbiological diagnosis, as good as LL, with no significant difference (95% CI; -0.214 - 0.274, p = 0.4). But TCB showed tendency for reliability over FNA (95%CI; - 0.20 to 0.42, p=0.07). This study tends to recommend that LL should not be utilized unless surgical intervention for other indications other than sampling is deemed necessary (Fig. 1).

Inflammatory parameters showed improvement in the oral treatment group at the end of six weeks therapy at least as good as parenterally treated patients ($p < 0.05$). Males predominate in VO (64.9%) in line with others; the majority of this population was elderly but about a decade younger

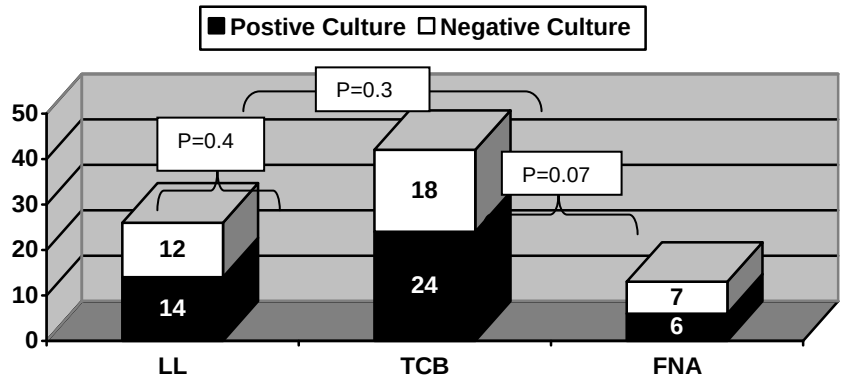

Fig. 1. Comparison among the three diagnostic methods in yielding a positive culture
Legend: Numbers on bars are in absolute value, LL: Limited Laminectomy, TCB: True Cut Biopsy, FNA: Fine Needle Aspiration

than previously published elsewhere where median age was 60 and 62.5 years. Diabetes mellitus was the commonest comorbidity (26.5%), (diabetes incidence in Jordanian adult population is 13.4%), two patients were diabetic with renal failure (2.7%). No sickle cell disease or intravenous drug users were identified, both are rare in Jordan.[1,3,10,19-22]

The location and extent of disease showed that majority were lumbar (60.9%), followed by lumbosacral (14.5%) followed by other sites. The extent of involvement was mostly multiple vertebrae in 61(88.4%) patient, all were adjacent; and the majority were two adjacent ones (69.7%) matching earlier studies. Adjacent vertebrae are jointly affected due to the mode of pathogens spread through blood supply as well as the anatomical extension.[10,18,19]

Mycobacterium tuberculosis followed by S. aureus including MRSA took the lead. One out of six cases of MRSA was from postoperative source and five cases were community acquired (CA-MRSA). CA-MRSA is now increasing in incidence; it is expected to contribute to the future burden of VO, especially in individuals who have been recently hospitalized, had hemodialysis, surgery, catheterization, and those in need of ambulatory medical care. Of note here is the presence of MTB (22.7%) and Brucellosis (9.0%) in considerable proportion, though the battle against both diseases is ongoing in Jordan and nearby Arab countries, it seems further efforts are needed. Some studies did not show tuberculosis among their patients; it is imperative to look at ones' regional data for management that is more precise rather than relying on data from other regions with different epidemiology.[3,10,12-17,23]

The imaging investigation mostly utilized was MRI. The number of vertebral bodies involved is less in pyogenic than in tuberculous VO, and the paravertebral abscesses are smaller, probably due to the insidious onset of tuberculosis and its propensity not to induce intense inflammation for it lacks endotoxins and exotoxins, in our patients all had two or more vertebrae involved with two patients had abscesses on presentation. In our experience, bone scan may be needed in MRI borderline cases. Should be there a contraindication to MRI then CT scan is a useful option, however CT is less sensitive than MRI for the detection of epidural abscesses or soft tissue lesions. In our review of CT scan studies, it was described as diagnostic in 53.3% of patients. Plain radiological investigation was found earlier not sensitive in VO diagnosis, even Colmenero et al. found that plain radiography was repeatedly normal throughout the entire evolutive course in 7/219 (3.1%) patients, six had brucellosis, and one had tuberculous VO.[4,6,11,16,19,25]

ESR lacks specificity but is useful in follow up, it showed that both orally-treated and parenterally-treated groups demonstrated similar improvement between the start and at the end of six weeks ($p < 0.05$), though patients' numbers were small to make a firm conclusion.[18,19]

Conclusion

TCB is a reliable procedure in yielding microbiologic diagnoses especially if surgical intervention was not found necessary. However, the initial antimicrobial treatment in the first six weeks is parenteral, but this study threw light that it may be in some cases replaced by oral therapy, or shorter

parenteral course may be administered (two weeks) and to follow that by oral treatment. In the era of some oral antimicrobials with descent bone concentration and spectrum, that covers the concerned potential pathogens; larger interventional studies are needed to address this point, as it bears significant cost effectiveness in sources limited patients and countries, and better patient compliance. The shortcoming of our study is that we did not adjust for the difference in diseases severity, comorbidities or different pathogens among the therapy groups, the patients' number were small, and due to the nature of the study, specific oral antimicrobial agents were not tested against specific parenteral ones. Furthermore, a randomized controlled study knows how to answer the outcome more precisely and highly needed.

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