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Diagnosis, management and outcome of clinically-suspected spinal infection

Roberto Luzzati [a,*], Donatella Giacomazzi [a], Maria Chiara Danzi [c], Leonello Tacconi [b], Ercole Concia [c], Sandro Vento [c,1]

[a] *Unit of Infectious Diseases, University Hospital, Via Stuparich 1, 34125 Trieste, Italy*
[b] *Unit of Neurosurgery, University Hospital, Via Stuparich 1, 34125 Trieste, Italy*
[c] *Unit of Infectious Diseases, University Hospital, Piazzale Scuro, 37100 Verona, Italy*

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Summary *Objectives:* Spontaneous spinal infection (SI) is a quite rare but serious entity. This study aimed to evaluate outcome and follow-up data of SI cases without a microbiological diagnosis (suspected SI).
Methods: We undertook a retrospective, comparative study of 82 spontaneous SI cases in adults presenting over an 11-year period to two Italian hospitals.
Results: The diagnostic yields of blood culture, percutaneous needle biopsy of spine, and surgical sample culture were 43.6%, 72.7%, and 91.6%, respectively. Overall, causative organisms were identified in 60 (73.2%) cases, the most frequently isolated pathogens being *Staphylococcus aureus* and *Mycobacterium tuberculosis*. The median diagnostic delay was similar ($p = 0.39$) in pyogenic (1 month) and suspected (0.5 month) SI cases, and longer in tuberculous cases (4 months) than in the other SI case groups ($p = 0.069$ and $p = 0.062$, respectively). All patients received antibiotic treatment, and 21 (25.5%) underwent surgery, that was required more frequently in tuberculous (40.7%) than in pyogenic (25.0%) and suspected SI cases (9.1%) ($p = 0.028$). Of 67 patients who completed a 1-year follow-up period, 24 had persisting painful disability that was more frequent in tuberculous (66.7%) cases than in pyogenic (21.7%) and suspected SI (15.0%) cases ($p = 0.03$).
Conclusions: Although a microbiological diagnosis was not achieved in nearly a quarter of SI cases, both diagnostic delay and outcome were similar to those of pyogenic SI cases. Earlier recognition of tuberculous SI is mandatory, as this is associated with the highest long-term morbidity.

* Corresponding author. Tel.: +39 040 3992591; fax: +39 040 3992652.
E-mail address: roberto.luzzati@aots.sanita.fvg.it (R. Luzzati).
[1] Present address: Infectious Diseases Unit, Ospedale ''Annunziata'', Via Migliori, 87100 Cosenza, Italy.

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Introduction

Spinal infections (SI) encompass a spectrum of distinct disease entities such as septic discitis, vertebral osteomyelitis, and epidural abscess, caused by a wide variety of organisms. Vertebral osteomyelitis represents approximately 2–7% of all cases of osteomyelitis.[1,2] In recent years, a rise in the incidence of pyogenic and nonpyogenic SI has been reported in many institutions,[3–6] as a consequence of an increasing number of individuals with predisposing factors such as advanced age, diabetes mellitus, chronic renal or liver disease, intravenous drug use, HIV infection, long-term steroid use, malignancy, chemotherapy, severe trauma, previous surgery. *Staphylococcus aureus* is far the most common etiologic agent of spontaneous SI, followed by aerobic gram-positive cocci and gram-negative bacilli.[7–10] *Mycobacterium tuberculosis* accounts for a significant number of SI not only in developing but also in industrialized countries, although often in immigrants from developing countries.[7,10–12] It has been estimated that tuberculous SI (T-SI) represents 50% of cases of skeletal tuberculosis,[13] and 1.7% of all cases of tuberculosis.[14] *Brucella* spp. accounts for a considerable number of cases of SI in endemic areas, such as Middle East and Mediterranean countries.[10,15,16] SI diagnosis is suggested by the presence of unremitting back or neck pain, which is relieved by neither rest nor analgesics, sometimes in combination with fever and neurological deficit. Diagnosis is supported by laboratory data and appropriate imaging changes (plain radiography, CT-scan, and MRI) but can be confirmed only by isolation of the causative organism or histological evidence (blood culture or tissue biopsy).[3] In a review of the literature published 30 years ago, only 25% of blood samples, 70% of spine needle biopsy and 86% of open biopsy samples yielded positive cultures.[17]

Even in more recent studies,[6–9] the identification of a causative pathogen proved impossible in a number of cases, and empirical antibiotic therapy had to be used.[3] Few data are available in the literature on features and outcome of SI cases without a microbiological diagnosis.[18,19] In this report, we present the results of a retrospective analysis of patients with spontaneous SI of undefined etiology compared to patients with pyogenic and tuberculous cases.

Patients and methods

Study population

The study included all consecutive adult patients (aged $\geq$18 years) diagnosed with SI between January 1995 and December 2005 at the University Hospitals of Trieste and Verona, Italy. Both hospitals are tertiary care referral centers located in two metropolitan areas in northeastern Italy, with a population of about 200,000 and 700,000 respectively.

Inclusion criteria and definitions

SI diagnosis was based on the presence of back or neck pain unrelieved by rest or analgesics, or of fever and/or neck/back pain with neurological deficit on physical examination, together with laboratory (elevated values for erythrocyte sedimentation rate and C-reactive protein) and MRI abnormalities.[20] An etiological diagnosis of SI was defined through identification of the causative microorganism from culture of a spine sample obtained by CT-guided percutaneous needle biopsy, or of a surgical sample from paravertebral sites, or from blood cultures (at least 2 separate sets of blood cultures in the case of common skin contaminants, such as coagulase-negative staphylococci, *Propionobacterium acnes*, diphteroids). Similarly, diagnosis of SI was considered definite when histopathological findings suggestive of infection (e.g., caseating granuloma for tuberculosis) were observed in a biopsy sample from spine or paravertebral sites. Suspected SI was considered, in the absence of microbiologic or histopathologic confirmation, when suggestive clinical features, appropriate MRI changes, and elevated inflammatory markers (erythrocyte sedimentation rate and C-reactive protein) were found and a positive clinical response to antimicrobial therapy was obtained. Patients with prior spinal instrumentation or surgery, or with recent penetrating trauma to the spine were excluded.

Data collection

The medical records were reviewed for demographic data, potential predisposing factors or underlying diseases, presenting signs and symptoms, diagnostic delay between onset of suggestive spine symptoms and time of imaging diagnosis, presenting level of spinal involvement including anatomic extension, inflammatory markers including white cell count (WCC), erythrocyte sedimentation rate, and C-reactive protein at diagnosis, serological status for brucellosis, microbiological and histological results, and therapeutic management including duration of antibiotic therapy and eventual surgical intervention.

Laboratory methods

When a rapid etiologic diagnosis by blood or surgical sample cultures had not been obtained, CT-guided percutaneous needle biopsy of spine had been proposed to the patient. Biopsies were obtained from the disk and/or the vertebral plates or body using a Lee-Lok bone marrow biopsy needle (Lee Medical Ltd, Minneapolis, USA) or an ABC-200 Elson bone needle (Williams Cook, Bjaeverskov, Denmark). Biopsy samples were divided into two parts for routine microbiologic and histopathological evaluations. In addition, every spinal sample, as well as those from any other site, were stained with Ziehl–Neelsen stain and cultured for 8 weeks on Lowenstein–Jensen and/or Middlebrook medium. Informed consent was obtained from each patient prior to both CT-guided percutaneous needle biopsy of spine or any surgical procedure.

Outcome and follow-up

Patients were constantly monitored by two of the authors (DG or MCD) until conclusion of antibiotic treatment, and thereafter at least every three months for one year or longer when needed. Outcomes were classified as: 'recovery', survival and disappearance of all signs and symptoms of active infection