A Seven-Year Prospective Study on Spondylodiscitis: Epidemiological and Microbiological Features

C. D'Agostino, L. Scorzolini, A.P. Massetti, M. Carnevalini, G. d'Ettorre, M. Venditti, V. Vullo, G.B. Orsi

Abstract

Background: The aim of this paper was to enlarge the available knowledge on clinical and etiological aspects of patients affected by spondylodiscitis.

Patients and Methods: All patients with spondylodiscitis admitted between January 2001 and December 2007 at the 1,300-bed University Hospital "Policlinico Umberto I" of Rome, Italy, were followed. Demographic characteristics, underlying diseases, invasive procedures, imaging studies, isolated microorganisms, treatment, complications, and outcome were recorded.

Results: Eighty-one patients of mean age 57.7 ± 14.7 years with lumbosacral (72.8%), thoracic (14.8%), and cervical tract (12.3%) site of infection were included, of which 38 developed community-acquired (CA) spondylodiscitis and 43 developed hospital-acquired (HA) spondylodiscitis. Underlying disease was present in 49.4% of patients. HA spondylodiscitis was diagnosed earlier (46.8 ± 49.7 days) than CA spondylodiscitis (65.0 ± 55.4 days) ($P < 0.05$). The most frequently isolated microorganisms were *Staphylococcus aureus* (28 strains, 43.1%), coagulase-negative staphylococci (CNS) (eight strains, 12.3%), *Pseudomonas aeruginosa* (eight strains, 12.3%), and three methicillin-resistant *S. aureus* (MRSA) strains were isolated in CA spondylodiscitis. Fungi and yeasts, isolated in six patients, represented 9.2% of all strains but 17.6% when considering only HA spondylodiscitis. Over 85% of patients were managed by conservative treatment alone, and the treatment time depended on clinical and laboratory evidence. Poor outcome was recorded in 12 (14.8%) patients, and was associated with neurological deficit symptoms (relative risk [RR] 2.87; 95% confidence interval [CI] 1.02–8.07; $P < 0.05$) and the time between diagnosis and the onset of symptoms ≥ 60 days (RR 2.65; 95% CI 0.92–7.59; $P < 0.05$).

Conclusions: Infectious spondylodiscitis affects most frequently the elderly population, who are more exposed to healthcare contacts. Consequently, the infection etiology includes a growing proportion of multi-resistant bacteria and fungi.

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Introduction

Spondylodiscitis is a rare disease accounting for 2–7% of all cases of pyogenic osteomyelitis, with incidence varying from 1 per 100,000/year to 1 per 250,000/year [1, 2]. However, there is evidence that the incidence is rising due to longer life expectancy for patients with chronic debilitating disease, immunosuppressive therapy, increasing use of indwelling devices, and spinal surgery [3–5].

Delay in diagnosis can result in more severe outcome [6] and is mostly due to the insidious onset of aspecific symptoms (neck or back pain, not always fever), and physicians are often unaccustomed to think about the diagnosis [2, 7].

Also, in many patients, clinical and imaging findings suggest the diagnosis before microbiological confirmation is obtained, and a causative organism remains unknown in up to 40% [2, 6, 8–14] of patients with typical features of pyogenic discitis, causing greater difficulty for the physician in selecting the most appropriate antimicrobial.

Therefore, the aim of the study was to describe the clinical profile, predisposing risk factors, and microorganism epidemiology of patients affected by spondylodiscitis in order to enlarge our knowledge and improve therapeutic management.

Methods

All patients with spondylodiscitis admitted between January 2001 and December 2007 at the 1,300-bed teaching hospital University Hospital "Policlinico Umberto I" of Rome, Italy,

C. D'Agostino, L. Scorzolini, A.P. Massetti, M. Carnevalini, G. d'Ettorre, M. Venditti, V. Vullo
Dept. of Infectious Diseases and Tropical Medicine, University "La Sapienza" Rome, Rome, Italy
G.B. Orsi *(corresponding author)*
Dept. of Public Health Sciences, University "La Sapienza" Rome, Piazzale Aldo Moro 5, 00185 Rome, Italy; Phone: (+39/06) 49914553, Fax: 4454845, e-mail: giovanni.orsi@uniroma1.it

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were included and specifically followed up for 1 year. A diagnosis of spondylodiscitis was made on clinical, radiological, and microbiological grounds, with patients fulfilling the following criteria [2, 15]:

(1) Clinical symptoms suggestive of spondylodiscitis (back pain unrelieved by rest; irradiated pain +/– neurological deficits +/– fever) and laboratory abnormalities: complete white blood cell count (WBC), erythrocyte sedimentation rate (ERS), and C-reactive protein (CRP) level.
(2) Abnormal magnetic resonance imaging (MRI) or computed tomography (CT) scan features compatible with infection of the spine.
(3) Isolation of the causative microorganism and/or typical histologic pattern from percutaneous disk or epidural abscess puncture or biopsy.

Patients with known or presumptive diagnosis for tuberculous or brucellar spine infection were excluded (all patients were screened with a brucellar serology test).

The study was approved by the hospital ethical committee.

For each patient, the following information was recorded: demographic characteristics, underlying diseases, clinical presentation, invasive procedures, laboratory data, radiologic imaging, microbiological findings, eventual surgical intervention, treatment, complications, and outcome at follow up.

All spondylodiscitis were classified into community-acquired (CA) spondylodiscitis or hospital-acquired (HA) spondylodiscitis when symptoms and signs of onset occurred within 48 h from hospital admission. The latter was identified as non post operative HA spondylodiscitis and post operative HA spondylodiscitis when the onset of symptoms and signs was within 1 year from spinal surgery.

Patients received appropriate antimicrobial treatment according to the isolated microorganism susceptibility test. A specific antibiotic therapy was administered intravenously and was eventually followed by oral treatment. When no microorganism was identified, based on the assumption that staphylococci are the leading cause of spondylodiscitis, an empirical antibiotic treatment was carried out by the association of glycopeptide and fluorochinolone ± rifampin for at least 6 weeks, eventually followed by oral treatment for another 6 weeks. Follow up examination assessing clinical features, laboratory data, and radiological pictures was carried out over a 1-year period. Special attention was given to the detection of poor outcome that was represented by sequelae (persistence of neurological symptoms), clinical relapse (improvement with relapse after antimicrobial administration without isolation of the original pathogen), and microbiological relapse (persistence of infection symptoms with isolation of the original pathogen).

Data Analysis

Statistical analyses were performed using Epi-Info (version 2005; CDC, Atlanta, GA, USA). The Chi-square was used to examine differences between groups. Statistical significance was defined as a *P*-value of less than 0.05. A univariate relationship was tested using the relative risk (RR) and its 95% confidence interval (CI_{95}).

Results

Demographics

The study included 81 patients (62.9% males, 37.1% females) of mean age 57.7 ± 14.7 years (range 18–97). Thirty-eight patients (46.9%) developed CA spondylodiscitis, 27 (33.3%) post operative HA spondylodiscitis, and 16 (19.8%) non post operative HA spondylodiscitis (Table 1).

Infection affected the most the lumbosacral tract (72.8%), followed by the thoracic (14.8%) and cervical tract (12.3%) (Table 1). Epidural abscess developed in 21 patients, while paravertebral abscess was observed in 15 (Figure 1). Only four iliopsoas abscesses were observed, all of which were associated with paraspinal abscess (Figure 2).

Risk Factors

The underlying diseases are illustrated in Table 1. An extravertebral infection was found in 28 patients (34.6%), varying from 62.5% in non post surgical HA spondylo-

Table 1
Demographic characteristics.

	CA spondylodiscitis	HA spondylodiscitis without spinal surgery	HA spondylodiscitis with spinal surgery	Total
No. of patients (%)	38 (46.9%)	16 (19.8%)	27 (33.3%)	81
Males	29 (56.9%)	9 (17.6%)	13 (25.5%)	51
Females	9 (30.0%)	7 (23.3%)	14 (46.7%)	30
Age (years)	56.7 ± 13.7	63.9 ± 16.0	55.4 ± 14.7	57.7 ± 14.7
Site of infection				
Cervical tract	3 (30.0%)	6 (60.0%)	1 (10.0%)	10
Thoracic tract	9 (75.0%)	3 (30.0%)	0	12
Lumbosacral tract	26 (44.1%)	7 (11.8%)	26 (44.1%)	59
Risk factors	47 (58.0%)	23 (28.4%)	11 (13.6%)	81
Liver	11 (84.6%)	2 (15.4%)	0	13
Devices	3 (25.0%)	6 (50.0%)	3 (25.0%)	12
Diabetes	6 (60.0%)	2 (20.0%)	2 (20.0%)	10
Malignancies	3 (30.0%)	5 (50.0%)	2 (20.0%)	10
Endocarditis	6 (85.7%)	1 (14.3%)	0	7
Cardiovascular	4 (57.1%)	2 (28.6%)	1 (14.3%)	7
Other	14 (63.7%)	5 (22.7%)	3 (13.6%)	22

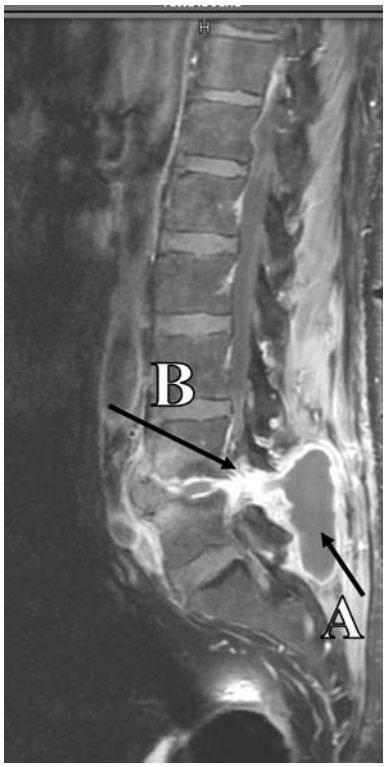

Figure 1. Sagittal magnetic resonance imaging (MRI) scan of the lumbosacral spine shows L4–L5 posterior paravertebral abscess (*A*) with spinal cord compression (*B*).

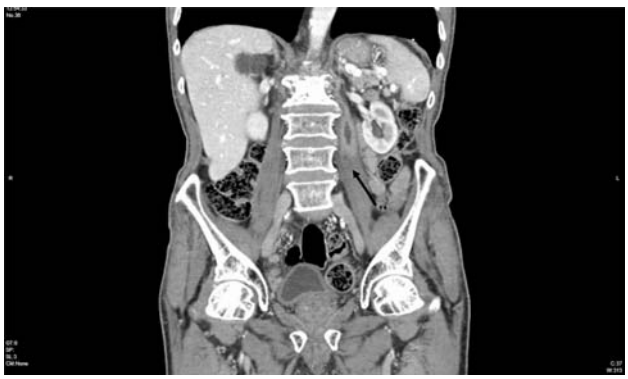

Figure 2. Computed tomography (CT) scan of the lumbosacral spine shows L1–L2 (spondylodiscitis in vertebroplasty) with left iliopsoas abscess (20 × 46 mm diameter).

discitis to 42.1% in CA spondylodiscitis and 7.4% in HA spondylodiscitis after spinal surgery.

Clinical Presentation

The time between diagnosis and the onset of symptoms had a mean of 55.4 ± 52.9 days and a median of 30 days. Overall, HA spondylodiscitis was diagnosed significantly ($P < 0.05$) earlier (46.8 ± 49.7 days) than CA spondylodiscitis (65.0 ± 55.4 days).

Back pain was the most commonly referred symptom (97.5%), followed by fever 76.5% (> 38°C in 58.0%, > 37°C, and ≤ 38°C in 18.5%), radicular pain (64.2%), and neurological deficit (14.8%). Although not significant, the latter was more frequent among CA spondylodiscitis (21.1%) than HA spondylodiscitis (9.3%). We found high WBC count (> 11.000) in 38.3%, increased ERS (> 50 mm/h value) and CRP (more than double the normal value) levels, respectively, in 67.9% and 95%, mild anemia (9.5 < Hb > 13) in 67.9%, and severe anemia (Hb < 9.5 g/dl) in 18.5%.

Imaging examination was carried out in almost all patients by MRI (98.8%). During the year-long follow up, we observed a radiological improvement in 80.2% of patients.

Microbiology

A causative microorganism for spondylodiscitis was isolated in 62 (76.5%) patients. CT-guided fine-needle aspiration (46 patients), blood cultures (42 patients), and intervertebral disk biopsy (10 patients) yielded bacterial growth in 76.1, 45.2, and 90% of patients, respectively. Agreement between cultures of fine-needle aspiration/biopsy and blood culture was obtained in eight patients.

Drainage of paravertebral/epidural abscess yielded isolation in five out of six patients (83.3%). Cephalorachidian fluid (CRF) was collected in just one case and yielded a positive culture. Etiology remained unknown in 19 cases; they were either negative cultures (10 cases) or the patient refused invasive procedures.

The majority of spondylodiscitis were monomicrobial (59 isolates, 95.2%) and Gram-positive bacteria were predominant (45 isolates, 69.3%), followed by Gram-negative bacteria (14 isolates, 21.5%) and yeasts (six isolates, 9.2%). The most commonly isolated microorganisms were *Staphylococcus aureus* (28 isolates, 43.1%), coagulase-negative staphylococci (CNS) (eight isolates, 12.3%), and *Pseudomonas aeruginosa* (eight isolates, 12.3%) (Table 2). Methicillin-resistant *S. aureus* (MRSA) were isolated in eight patients and three were CA spondylodiscitis, referring to preceding healthcare contact (2) and jail stay (1).

Fungi and yeasts were isolated in six patients (four *Candida* spp. and two *Aspergillus* spp.), representing 17.6% of all HA spondylodiscitis etiologies (Table 2). Three patients (A, B and C) affected by *Candida* spondylodiscitis presented various risk factors for fungemia (e.g., kidney failure, parenteral nutrition, central venous catheter [CVC], etc.), and in two of them (A and C), spondylodiscitis followed a preceding episode of onset fungemia (Table 3). Differently, one patient (D), without preceding fungemia and related risk factors, developed HA spondylodiscitis 2 weeks after vertebroplasty surgery for spinal collapse (L1–L2) by osteoporosis (Table 3).

Table 2
Microorganisms distribution.

Microorganisms	CA spondylodiscitis	HA spondylodiscitis without spinal surgery	HA spondylodiscitis with spinal surgery	Total
MRSA[a]	3	2	3	8
MSSA[b]	13	3	4	20
MR-CNS[c]	1	1	2	4
MS-CNS[d]	3	1	0	4
Streptococcus spp.	6	1	0	7
Pseudomonas aeruginosa	2	2	4	8
Candida spp.	0	3	1	4
Aspergillus spp.	0	0	2	2
Others	3	2	3	8
Total	31	15	19	65

[a] Methicillin-resistant *Staphylococcus aureus*
[b] Methicillin-sensitive *Staphylococcus aureus*
[c] Methicillin-resistant coagulase-negative staphylococci
[d] Methicillin-sensitive coagulase-negative staphylococci

Both *Aspergillus* HA spondylodiscitis cases were post operative and came from two different other hospitals.

Treatment and Outcome

Most patients (87.6%) received only medical treatment consisting of intravenous antimicrobials (mean duration 7.5 ± 4.9 weeks), followed in 69.1% by oral antibiotics (mean duration 6.1 ± 5.6 weeks). The antimicrobial treatment length was longer for *P. aeruginosa* (16.3 ± 3.9 weeks), followed by *Streptococcus/Enterococcus* spp. (14.3 ± 5.8 weeks), *S. aureus* (13.2 ± 7.2 weeks), and CNS (12.4 ± 7.5 weeks). Patients with *Candida* spp. were treated for 17.2 ± 12.6 weeks and the two patients with *Aspergillus* spp. for 30.5 ± 3.5 weeks (Table 3). The antimicrobial treatment length, depending on the isolated microorganism and time for the CRP level to return to normal, was decided by the physician caring for the patient. Only four patients received antimicrobial therapy before obtaining the microbiological results.

We observed a favorable long-term outcome in 65 (80.2%) patients, a poor outcome in 12 (14.8%), one of whom died, and four (4.9%) were lost to follow up. Poor outcome was represented by sequelae (6), clinical relapse (3), and microbiological relapse (3). A poor outcome was observed more frequently among non post surgical HA spondylodiscitis (37.5%) compared to CA spondylodiscitis (10.5%) and spondylodiscitis after spinal surgery (7.4%). The 12 patients with unfavorable outcome developed a spondylodiscitis infection by staphylococci (7), streptococci (1), *P. aeruginosa* (1), and *Candida* spp. (1). The three confirmed relapses (one death) were in patients with staphylococcal infection.

When we considered separately patients with and without microorganism isolation, no association with poor outcome was seen. Adverse outcome was not significantly associated with age, sex, comorbidity, and microorganism. Univariate analysis showed an association with neurological deficit symptoms (RR 2.87; 95% CI 1.02–8.07; $P < 0.05$) and the time between diagnosis and the onset of symptoms ≥ 60 days (RR 2.65; 95% CI 0.92–7.59; $P < 0.05$).

Discussion

As reported by others [4–7], spondylodiscitis affected the elderly more frequently, but with a male predominance only in the CA spondylodiscitis group, whereas among HA spondylodiscitis, there was an equal distribution between the sexes (Table 1).

Comorbidities, although recognized to increase the risk of pyogenic spinal infection [4, 16], were not an independent risk factor for a poor outcome.

As reported by others [5, 6], the time between diagnosis and the onset of symptoms ≥ 60 days was associated to poor outcome. All HA spondylodiscitis (median 30 days) were diagnosed significantly earlier than CA spondylodiscitis (median 45 days), confirming that prompt referral to experienced physicians shortens the time of diagnosis. Furthermore, neurological deficit was more frequent among CA spondylodiscitis than HA spondylodiscitis (21.1 vs. 9.3%), underlining how a longer time of diagnosis is a risk factor for unfavorable outcome.

Gram-positive bacteria outnumbered Gram-negative, and the most commonly isolated microorganisms were staphylococci (55.4%) [2, 6, 14, 17]. *S. aureus* remains the predominant causative microorganism and, in particular, MRSA was isolated from eight patients (Table 2). Of interest, three spondylodiscitis by MRSA were onset in the community; two patients referring preceding healthcare contact and one jail stay. This observation confirms also for disk space infections the importance to distinguish between healthcare-acquired infection (HCAI) and community-acquired infection (CAI) [18, 19].

Table 3
Characteristics of patients with fungal hospital-acquired (HA) spondylodiscitis.

Patient	Status	Age/sex	Predisposing condition for fungal infection	Site of infection	Organism cultured		Antimicrobial therapy	Therapy (weeks)	Management	Outcome
					Tissue	Blood				
A	NPO*	60/F	Spondyloarthrosis, CVC, parenteral nutrition, colectomy, kidney failure	D12–L4	*Candida albicans*	*Candida albicans*	Fluconazole 400 mg/day	36	Nonoperative	Sequelae
B	NPO*	53/M	Leukemia, immunosuppressive therapy	L2–L3	*Candida albicans*	*Candida albicans*	Fluconazole 400 mg/day	9	Spinal surgery	Recovery
C	NPO*	66/F	Kidney cancer, CVC, endocarditis	C6–C7	*Candida glabrata*	*Candida glabrata*	Liposomal amphotericin B 5 mg/kg/day	12	Nonoperative	Recovery
D	PO**	74/M	–	L1–L2	*Candida albicans*	–	Fluconazole 400 mg/day, liposomal amphotericin B 5 mg/kg/day	12	Nonoperative	Recovery
E	PO**	60/M	–	L4–L5	*Aspergillus fumigatus*	–	Voriconazole 12 mg/day	28	Nonoperative	Recovery
F	PO**	61/M	Vesical tumor	L4–L5	*Aspergillus* spp.	–	Voriconazole 12 mg/day	33	Nonoperative	Recovery

*Non post operative HA spondylodiscitis
**Post operative HA spondylodiscitis

Seven (8.6%) patients developed endocarditis (six CA spondylodiscitis and one non post surgical HA spondylodiscitis), and the isolated microorganisms were streptococci (3), staphylococci (3), and *Candida* spp. (1). As spondylodiscitis may be a complication of an infective endocarditis, particularly in drug abusers, in case of pre-existing heart diseases, some authors recommend the routine use of echocardiography in all cases of spondylodiscitis to exclude infective endocarditis [20–22].

Of interest, filamentous fungi and yeasts represented 9.2% of all strains, and emerged as the second (17.6%) most commonly isolated microorganism after staphylococci when considering only HA spondylodiscitis (Table 2). This was unexpected because, in spite of the increasing frequency of candidemia, *Candida* is still a relatively uncommon cause of spinal infection with a limited number of reported cases [23–26].

Most patients with vertebral osteomyelitis by *Candida* carried various predisposing factors [26] (Table 3), and some postulate that the intervertebral disk may represent a privileged site within which fungi are sheltered from antimicrobial and immunological clearance [23]. Surprisingly, in one patient, candidal spondylodiscitis did not follow candidemia but, instead, surgery, suggesting the direct invasion of fungus into the disk space during previous spine surgery or set in when this site was vulnerable [24]. Such association has been rarely reported in the literature [24, 27].

We also observed two post surgical HA spondylodiscitis due to *Aspergillus* spp. (Table 3). Obviously, the main risk factor was the surgical procedure, but, also, one patient was immunocompromised with bladder cancer and nephrostomy.

Most pyogenic spinal infections (> 85%) were managed successfully by conservative measures alone, requiring a minimum of 6 weeks of intravenous antibiotic therapy [14]. When patients improved, but without attaining baseline levels of inflammatory biomarkers, treatment was continued for at least 12 weeks by oral therapy after the completion of parental therapy [28]. Debridement in fungal spondylodiscitis was limited to only one patient [27].

Due to the rarity of spondylodiscitis, no randomized controlled trials on antimicrobial therapy have been carried out [28]. Therefore, the therapy is principally based by physicians on considerations including antimicrobial activity against known or likely pathogens, the ability to penetrate bone and disk tissue, and the side effects profile [4]. However, in our opinion, the low mortality rate [4], as only one patient died, due to the consequences of extravertebral infection, and the limited number of patients with poor outcome (< 20%) are encouraging elements to persist on the adopted treatment approach. Furthermore, all patients with fungi and yeasts received only antifungal treatment and five out of six recovered completely. The single case (patient A in Table 3) who presented a sequelae had been suffering from a large destruction of bone tissue.

We found that neurologic deficit symptoms were a prognostic unfavorable sign for an adverse outcome. We could not explain why we observed a poor outcome in over one-third of non post surgical HA spondylodiscitis.

Our study has both strengths and potential limitations. Even though the study was carried out in a single center, it provided some useful up-to-date information on spondylodiscitis etiology. Unfortunately, the study design did not include the distinction between community-acquired infections and community-onset healthcare-associated infections. Also, the follow up lasted for only 1 year, limiting the possibility to monitor eventual very late sequelae.

In conclusion, infectious spondylodiscitis affects most frequently the elderly population, who are more exposed to healthcare contacts. Consequently, the infection etiology includes a growing proportion of multi-resistant bacteria (methicillin-resistant staphylococci and Gram-negative bacilli) and fungi.

The majority of spondylodiscitis cases may be managed successfully by conservative measures alone, and favorable results could be further improved with earlier diagnosis and prompt targeted antimicrobial therapy.

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