International Journal of Infectious Diseases (2009) **13**, 564—569

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Spontaneous spondylodiscitis: presentation, risk factors, diagnosis, management, and outcome☆

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Received 17 June 2008; received in revised form 8 August 2008; accepted 27 August 2008
Corresponding Editor: William Cameron, Ottawa, Canada

KEYWORDS
Spondylodiscitis;
Back pain;
Magnetic resonance imaging;
Diabetes mellitus;
Staphylococcus aureus

Summary
Background: Spontaneous spondylodiscitis is an uncommon disease, which may result in serious complications with potentially high morbidity and mortality. We conducted a prospective case study over a 2-year period in order to analyze the clinical features, approaches to management, and outcome of spondylodiscitis.
Methods: Eight consecutive patients (four men, four women; age range 53—82 years) suffering from spondylodiscitis were identified during the study period. Parameters recorded included: demographics, past medical history, predisposing factors, presenting signs and symptoms, spinal level and extension of the infection, laboratory indices of inflammation, microbiological testing, radiological assessment, kind and duration of treatment, follow-up magnetic resonance imaging (MRI) studies, and outcome.
Results: Duration of symptoms varied from 14 to 90 days. All patients had back pain; fever $\geq$38 °C was present in 5/8 (62.5%) and neurological findings in 6/8 (75%). Diabetes mellitus was identified in six (75%). Most of the patients had elevated laboratory markers of inflammation. At the initial MRI, 12 anatomical levels were found. The microorganism was identified in 7/8 by blood or bone marrow cultures (50% *Staphylococcus aureus*). None of the patients underwent surgical intervention. Seven patients (87.5%) recovered to full activity; follow-up MRI study results were not always in parallel with the clinical improvement of patients.
Conclusions: Spontaneous spondylodiscitis should be considered in every patient with back pain accompanied by fever and laboratory markers of inflammation. The major predisposing risk factor seems to be uncontrolled diabetes. MRI appears to be the method of choice for confirming

☆ This work was presented in part as an abstract at the 32nd Congress of the European Society of Neuroradiology, Genoa, Italy, September 21—23, 2007; *Neuroradiology* 2007;**49**(Suppl 2):S127.

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doi:10.1016/j.ijid.2008.08.025

diagnosis. Timely and accurate diagnosis along with prompt administration of antibiotics appears mandatory for a favorable outcome and avoidance of surgical intervention.

Introduction

Infectious spondylodiscitis, or septic discitis, is an uncommon infectious condition in which symptoms may be non-specific, including fever, local tenderness, and neurological signs when deformity of the affected structures has developed.[1,2] The course may be acute or chronic, but the lack of specific symptoms usually results in delayed diagnosis leading to potentially high morbidity and mortality.[3] In most cases the affected patients have one or more predisposing underlying conditions, such as diabetes mellitus, alcoholism, HIV infection, a spinal abnormality or intervention, or a potential local or systemic source of infection.[3,4]

The aim of the present prospective study was to determine the whole spectrum of spondylodiscitis, including the clinical manifestations of the disease, the underlying risk factors, and the diagnostic work-up required to reach a timely and correct diagnosis, as well as the management, follow-up, and the outcome of a consecutive series of eight patients who were admitted to the Department of Medicine of the Medical School, University of Thessaly, Central Greece over a 2-year period (2005—2007).

Materials and methods

During the study period we identified eight patients with spontaneous spondylodiscitis. Diagnosis was based on clinical presentation, high laboratory indices of inflammation (white blood cell count (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)), and identification of the causative organism from blood or bone marrow cultures, confirmed by magnetic resonance imaging (MRI) findings.

Demographic, clinical, laboratory, and radiological data were collected prospectively for each case. The management of the disease and clinical, laboratory, and MRI follow-up studies of the patients were also recorded. MRI findings suggestive of spondylodiscitis included increased signal of the intervertebral disc on T2 images, vertebral body marrow edema, vertebral body and disc enhancement, epidural or paraspinal inflammation, and canal compromise. At the follow-up MRI studies performed 4—6 weeks after the initial MRI, imaging characteristics were categorized as improved, unchanged, or worsened compared to the initial study. The ethics committee of the Medical School, University of Thessaly, approved the study protocol.

Results

Patient characteristics

The epidemiological and clinical data of the patients are shown in Table 1. Seven patients had been treated with analgesics, while two had received antibiotic treatment. One patient (patient 4) developed catastrophic antiphospholipid syndrome.[5,6] Physical examination revealed neurological findings in six patients, namely decreased sensation below the spinal level of infection, decreased tendon reflexes of the lower limbs, and Lasegue's sign. None of the patients was under immunosuppression, had chronic spinal disease, history of chronic back pain, or had undergone any spinal surgical procedure in the past. Diabetes mellitus was defined as uncontrolled in all six diabetic patients as attested by the high concentrations of glycosylated hemoglobin A_1.

Table 1 Epidemiological and clinical data of patients at presentation.

Patient	Sex	Age (years)	Initial prevailing symptom	Fever (≥38 °C)	Local spine sensitivity	Duration of symptoms,[a] days	Diabetes mellitus	Underlying condition	Previous treatment
1	F	53	Back pain	No	Yes	90	Yes	Scabies	NSAIDs, antibiotics
2	M	82	Back pain	Yes	Yes	30	Yes	Squamous cell carcinoma, CHD	Antibiotics
3	M	65	Back pain	Yes	Yes	20	Yes	CHD, hypertension	NSAIDs
4	F	59	Back pain	No	Yes	14	Yes	Hypertension	NSAIDs
5	M	82	Back pain	No	No	45	No	Hypertension, COPD, benign prostatic hyperplasia	NSAIDs
6	F	63	Back pain	Yes	Yes	45	Yes	Asthma	NSAIDs
7	M	57	Back pain	Yes	Yes	40	Yes	Hypertension	NSAIDs
8	F	63	Back pain	Yes	Yes	20	No	Decompensated HCV-related cirrhosis	Paracetamol

M, male; F, female; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; HCV, hepatitis C virus; NSAIDs, non-steroidal anti-inflammatory drugs.

[a] One or more of the following symptoms: back pain, fever, chills, rigor, sweats, dyspnea, anorexia, weight loss, arthralgias, proximal muscle weakness of the lower limbs.

Table 2 Laboratory data, causative agents, MRI findings, treatment, and follow-up of the patients with spondylodiscitis.

Patient	Initial laboratory data			Laboratory data at discharge			Causative agent	Level of lesions	T2 SI increase	DE	BM	VB Gado+	Management	Pain relief (days)	Mobilization (days)	Follow-up MRI (4—6 weeks)
	WBC ($\times 10^9$/l)	CRP (mg/dl)	ESR (mm/1h)	WBC ($\times 10^9$/l)	CRP (mg/dl)	ESR (mm/1h)										
1	13.3	19.7	79	5.2	0.9	15	Undefined	T10—11	+	+	+	+	Vancomycin IV (45 days); oral ciprofloxacin + rifampin for 6 months	33	45	Improved
2	4.9	19.7	61	5.1	0.9	21	*Staphylococcus aureus*	L1—2 T9—10	+ +	— —	+ —	+ —	Teicoplanin IV (42 days); oral ciprofloxacin + rifampin for 7 months	16	70	Stable Improved
3	9.3	6.9	83	8.6	3.0	35	*Brucella melitensis*	T12—L1 L4—5	— +	— —	+ +	+ —	Streptomycin IM (21 days) + oral rifampin + doxycycline for 2 months	30	14	Stable Stable
4	29.8	35	119	5.9	3.1	48	*Staphylococcus aureus*	T11—12 L4—5	+ +	+ +	+ +	+ +	Teicoplanin IV (90 days); oral ciprofloxacin for 15 months	17	73	Improved Stable
5	7.1	9.9	61	6.9	2.8	21	*Pseudomonas aeruginosa*	T6—7 T11—12	— +	+ +	+ +	+ +	Ticarcillin/clavulanic acid IV (45 days); oral ciprofloxacin for 10 months	14	42	Stable Stable
6	19.1	28	63	5.9	0.8	23	*Staphylococcus aureus*	L3—4	+	+	—	+	Vancomycin IV (45 days); oral ciprofloxacin + rifampin for 10 months	15	30	Worsened[a]
7	10.6	3.7	47	4.9	0.1	22	*Staphylococcus aureus*	L3—4	+	+	+	+	Vancomycin IV (42 days); oral ciprofloxacin + rifampin for 7 months	10	20	Improved
8	30.7	2.3	12	2.9	0.1	14	*Enterococcus faecalis* and *Escherichia coli*	L3—4	—	—	+	+	Teicoplanin IV (42 days) and meropenem IV (14 days); oral ciprofloxacin for 10 months	30	35	Improved

WBC, white blood cell count; CRP, C-reactive protein (upper normal limit <1 mg/dl); ESR, erythrocyte sedimentation rate (upper normal limit < 20 mm/1 h); T, thoracic; L, lumbar; SI, signal intensity; DE, disc enhancement; BM, bone marrow edema; VB Gado+, vertebral body enhancement after gadolinium; MRI, magnetic resonance imaging; IV, intravenous; IM, intramuscular. Patients are numbered the same as in Table 1.

[a] There was worsening of all imaging findings except epidural and paraspinal infection, which were improved.

Imaging studies and identification of the causative agents

Plain films of the spine were not helpful. Technetium bone scans (Tc-99m-MDP), demonstrated abnormalities suggestive of infection in all of the patients; three patients initially underwent computed tomography (CT) scans of the lumbar spine; one study was negative. Using MRI studies we identified 12 anatomical levels of infection (Table 2).

The causative organism was identified in 7/8 (87.5%) patients. In four patients *Staphylococcus aureus* was identified, while *Brucella melitensis*, *Pseudomonas aeruginosa*, and a double infection due to *Enterococcus faecalis* and *Escherichia coli* were identified in the remaining three patients (Table 2). Patients 1, 3, 4, 6, and 7 had both epidural and paraspinal infections. Canal stenosis (%) was observed by MRI in patients 1, 4, and 7 (<25%) and patient 6 (>25%). The most likely portal of entry in cases with *Staphylococcus aureus* was the skin (particularly via crevices between the toes). The patient with brucellosis was a stockbreeder and had a positive history for contracting brucella — ingestion of unpasteurized dairy products and unsafe daily practices during his work, as he did not usually wear gloves when milking and shearing his animals or when lambing. In patient 5, we speculate that infection with *Pseudomonas aeruginosa* was due to a urinary infection as the same bacterium was identified in urine and blood cultures. Patient 8 with the double infection was suffering a urinary infection and spontaneous bacterial peritonitis due to the underlying decompensated cirrhosis, from which the bacteria disseminated hematogenously to the spine. No causative agent was identified in patient 1 as she had been treated previously with antibiotics. The diagnosis in this patient was based on the clinical features, the typical MRI findings, and the exclusion of other pathologies, as well as on the favorable outcome after antibiotic treatment with sharp response of the inflammatory markers and full clinical and MRI recovery followed by complete mobilization.

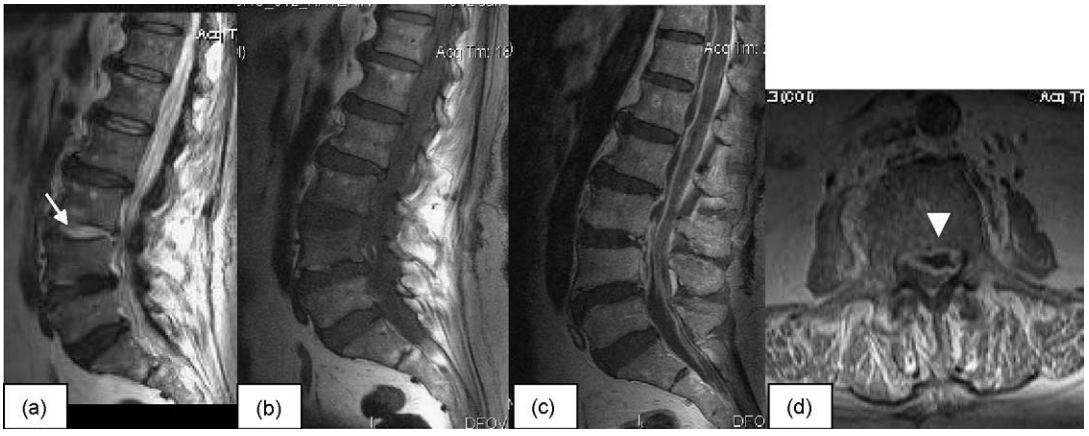

Figure 1 Initial MRI from patient 6: sagittal T2 (a), T1 (b), and post-gadolinium sagittal (c) and axial (d) T1 images show increased signal of the L3—L4 intervertebral disc (arrow), bone marrow edema of the adjacent vertebral bodies, and contrast enhancement of the vertebral body. There is paraspinal infection and extension of the infection to the epidural space up to the level of T11, producing canal stenosis (arrowhead).

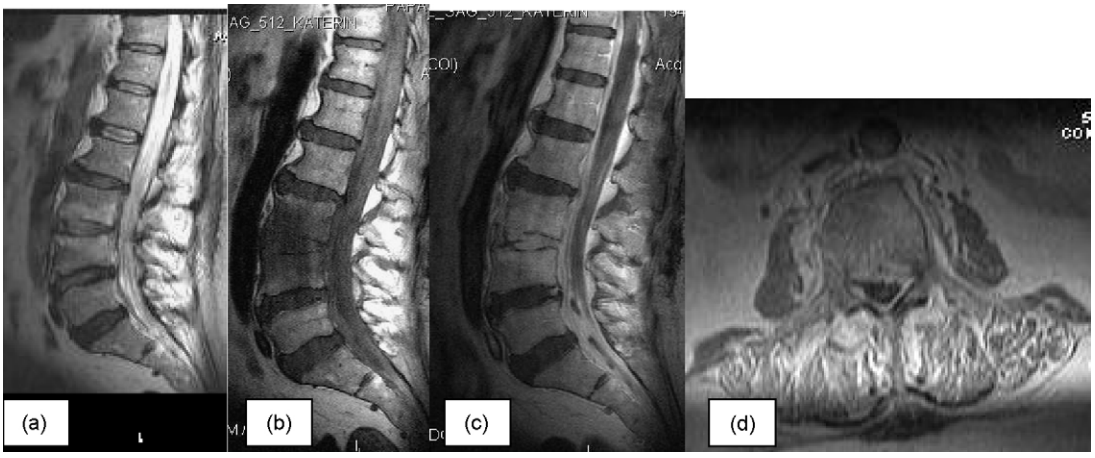

Figure 2 Follow-up MRI at 6 weeks from patient 6: sagittal T2 (a), T1 (b), and post-gadolinium sagittal (c) and axial (d) T1 images show improvement of the intervertebral disc signal on T2 images, more extensive bone marrow edema of the L3—L4 vertebral bodies, more extensive post-gadolinium enhancement of the vertebral body and the intervertebral disc, but improvement of the epidural and paraspinal abscesses.

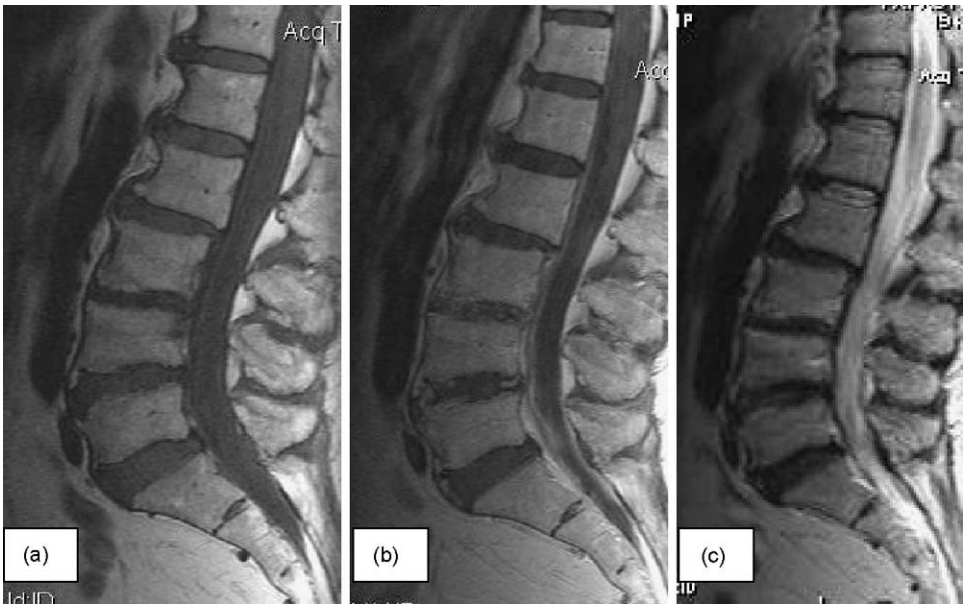

Figure 3 Follow-up MRI at 12 months from patient 6: sagittal T1 before (a) and after (b) contrast administration and T2 images (c). There are no signs of infection.

Patients 3, 4, 5, 6, and 8 completed antibiotic treatment, while the other three patients were still receiving antibiotics per os at the time of last follow-up in order to complete 10—12 months of treatment.

Management and follow-up of the patients

None of the patients needed a surgical intervention. All patients treated initially with intravenous antibiotics were then switched to an oral combination (usually ciprofloxacin and rifampin) (Table 2). One patient received vancomycin empirically against a possible infection due to *Staphylococcus aureus* as she suffered from scabies.

Bone marrow edema and increased T2 signal of the intervertebral disc persisted even at the 6-month follow up MRI (5/10 levels affected in patients who had completed 6 months of treatment) and 12-month MRI (3/6 levels affected in patients who had completed 12 months of treatment), though there was not any clinical or laboratory evidence of persistent disease. MRI imaging findings at presentation, at 6 weeks, and at 12 months from a representative case (patient 6) are shown in Figures 1—3.

Discussion

This study presents the whole epidemiological, clinical, laboratory, imaging, and long-term follow-up data, as well as the outcome in a group of eight patients with spontaneous spondylodiscitis. Back pain was the hallmark clinical manifestation of the disease (100%) irrespective of the causative microorganism.[2,7—9] Duration of symptoms and signs ranged from 14 to 45 days in 7/8 patients, with the exception of 3 months in one patient, which may reflect the under-diagnosis of this disease, as the clinical picture is quite non-specific leading to difficulties in its timely diagnosis, at least at the first medical evaluation.[10—15] Laboratory work-up revealed an acute phase response (elevated ESR, CRP, and leukocytosis) in most of our patients at the time of diagnosis.

The rate of positive blood cultures is around 50%, but it may be even lower.[1,2,7] Of note, all but one patient in our study had a positive blood culture. Spontaneous pyogenic spondylodiscitis usually spreads hematogenously from infections of the skin, subcutaneous tissues, and urinary tract.[16] Numerous underlying risk factors have been associated with the disease, such as diabetes mellitus, intravenous drug abuse, catheter-associated infections, surgical interventions, infective endocarditis, urinary tract infections, chronic alcoholism, and immunocompromised states.[2,9] Our report appears to support a relationship of diabetes mellitus with the development of spondylodiscitis.[17]

Radiological evaluation of patients by MRI appears to be the method of choice for detecting lesions of spondylodiscitis, particularly at the initial stages, showing as bone marrow edema, increased signal of the intervertebral disc on T2 images, and enhancement of the disc and the vertebral body after gadolinium administration.[1,2,7,18,19] However, we observed a lack of correlation between long-term follow-up MRI studies and the favorable treatment outcome of patients.[20]

Concerning the therapeutic strategy for spondylodiscitis, there is no clear consensus, as so far no randomized clinical trials of short-course or oral antibiotic regimens have been published.[1,2,7,12,15] As a result, the duration of antibiotic treatment varies widely both between and within centers.[3,12,15] Antibiotics are usually given intravenously for 4—6 weeks, including regimens against *Staphylococcus aureus* and possibly against Gram-negative bacteria until sufficient clinical improvement has been achieved, and CRP and ESR levels are reduced.[21] An additional oral course of at least 6 weeks is usually recommended.[15,22] However, even longer therapy may be needed because of delays in diagnosis resulting in the infection being similar to chronic osteomyelitis and where 6—8 weeks of therapy do not suffice.

In conclusion, our data suggest that infectious discitis should be considered in any patient with localized pain at any level of the spine, and especially in those who suffer from diabetes mellitus, and where their symptoms are accompanied by fever and indicators of an acute phase response. MRI has very good sensitivity, specificity, and diagnostic accuracy for confirming the clinical diagnosis and may be a valuable tool for the evaluation of treatment efficacy, though clinical improvement appears not always to correlate with the improvement in imaging findings. Early detection of the disease is important to avoid surgical interventions and in terms of prognosis as this condition is characterized by prolonged hospitalization and long-standing immobilization.[23]

Conflict of interest: No conflict of interest to declare.

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