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Clinical and Laboratory Characteristics of Infective Endocarditis When Associated with Spondylodiscitis

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Abstract Spondylodiscitis is rarely observed in association with infective endocarditis (IE). In the study presented here, 92 cases of definite IE were examined. Spondylodiscitis was present in 14 (15%) cases. The mean age of patients with spondylodiscitis was 69.1±13.6 years (range, 33–87 years). The male-to-female ratio was 8:6. Predisposing heart disease was found in nine (64.3%) cases. Back pain was reported in all cases. Spondylodiscitis was diagnosed before endocarditis in all cases. The infection affected the lumbar spine in 10 (71%) cases. A bacterium was isolated in all cases: group D *Streptococcus* (*n*=5; 35.7%), coagulase-negative *Staphylococcus* (*n*=4; 28.6%), and others (*n*=5). Endocarditis affected predominantly the aortic valve (43%). The outcome was favourable in 12 cases. No differences in clinical features, evolution of disease, or laboratory values were found between IE patients with and IE patients without spondylodiscitis. Spondylodiscitis does not appear to worsen prognosis of IE, although the need for cardiac valve replacement seems to be more frequent in IE patients with spondylodiscitis. IE should be included in the differential diagnosis in patients with infectious spondylodiscitis and risk factors for endocarditis. In such patients, echocardiography should be performed routinely.

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Introduction

Infective endocarditis (IE) is associated with a high risk of complications such as cerebral emboli, splenic infarction, glomerulonephritis, and/or rheumatologic manifestations. The common occurrence of rheumatic features in IE has been emphasized in many studies, with prevalence rates ranging from 25 to 44% [1, 2, 3, 4, 5, 6, 7]. Spondylodiscitis, however, is rarely observed [1]. The goals of our study were to evaluate the frequency of spondylodiscitis in patients with IE and to assess the clinical and laboratory features of IE when associated with spondylodiscitis.

Patients and Methods

A retrospective review of all patients with IE was carried out in the Department of Internal Medicine and Infectious Diseases in the university hospital of Poitiers, France (2,700 beds) from January 1990 through December 2000. Only patients with definite IE according to the Duke criteria were included [8]. The following data were analyzed at the time of diagnosis: demographic features, delay between the onset of symptoms and diagnosis of IE, predisposing heart disease and past personal history, clinical features (fever, other infectious localization), the affected valve, results of routine laboratory tests (including blood culture, liver and renal function, and inflammatory parameters), antimicrobial therapy, surgical procedures, if any, and evolution of disease. The patients were classified in two groups: group 1 consisted of patients without spondylodiscitis, and group 2 consisted of patients with spondylodiscitis.

Infectious spondylodiscitis was suspected in the case of back pain compatible with vertebral infection and/or stiffness and confirmed by plain radiography, bone scintigraphy, computed tomography scan, or magnetic resonance imaging. For each patient with spondylodiscitis, additional data were collected: delay between diagnosis of spondylodiscitis and diagnosis of IE, localization of spondylodiscitis, and length of treatment.

Continuous data were described as means and standard deviations, and categorical variables as percentages. Comparisons between two categories were made using the Student's *t* test for continuous variables. Categorical data were analyzed using the chi-square test. When the minimum expected value was less than 5, the chi-square test with Yates correction was used. Statistical significance was defined as $P \leq 0.05$. Calculations were performed with Epi Info 2000 software (Centers for Disease Control and Prevention, USA).

Table 1 Characteristics of spondylodiscitis in patients with infective endocarditis

Case no.	Age/sex	Predisposing condition	Location of discitis	Antibiotic treatment	Causative bacteria isolated from blood cultures
1	82/M	pacemaker	C2-C3	VAN + RIF	*Staphylococcus schleifferi*
2	55/F	none	L4-L5	CEF	*Streptococcus milleri*
3	33/M	none	D8-D9	OXA + OFL	*Staphylococcus aureus*
4	80/F	none	L1-L2	AMX + GEN	group D *Streptococcus*
5	72/M	pacemaker	L2-L3	OXA + RIF	*Staphylococcus epidermidis*
6	71/M	none	L2-L3	OXA + GEN	*Staphylococcus aureus*
7	78/M	pacemaker	D8-D9	OXA + RIF	*Staphylococcus epidermidis*
8	80/M	prosthetic valve	L3-L4	AMX + GEN	group D *Streptococcus*
9	87/M	prosthetic valve	L5-S1	CEF	*Streptococcus salivarius*
10	66/F	none	D7-D8	AMX + GEN	group D *streptococcus*
11	71/M	prosthetic valve	L2-L3	AMX + GEN	*Streptococcus sanguis*
12	64/M	pacemaker	L1-L2	OXA + GEN	*Staphylococcus epidermidis*
13	68/F	prosthetic valve	L4-L5	AMX + GEN	group D *Streptococcus*
14	61/F	pacemaker	L3-L4	AMX + GEN	group D *Streptococcus*

VAN, vancomycin; AMX, amoxicillin; OXA, oxacillin; RIF, rifampin; OFL, ofloxacin; CEF, ceftriaxone; GEN, gentamicin

Table 2 Demographic and epidemiologic features of 92 patients with infective endocarditis: 78 without spondylodiscitis (group 1) and 14 with spondylodiscitis (group 2)

Characteristic	Group 1 (*n*=78)	Group 2 (*n*=14)	*P* value
Mean age in years ±SD (range)	65.5±14.9 (16–90)	69.1±13.6 (33–87)	NS
Sex (M/F)	57/21	9/5	NS
No. of cases in patients >60 years	45 (57.7%)	12 (85.7%)	NS
Predisposing heart conditions			
Degenerative valve disease	18 (23.1%)	0	NS
Intracardiac device	25 (32.1%)	9 (64.3%)	0.04
Prosthetic valve	13 (16.7%)	4 (28.6%)	NS
Pacemaker	12 (15.4%)	5 (35.7%)	NS
Valve involvement			
Aortic	37 (47.4%)	6 (42.9%)	NS
Mitral	22 (28.2%)	3 (21.4%)	NS
Tricuspid	7 (9.0%)	0	NS
Pacemaker	12 (15.4%)	5 (35.7%)	NS
Mean delay to diagnosis in days (range)	38.1 (1–300)	42.6 (2–180)	NS

NS, nonsignificant

Results

During the study period, 92 patients presented with definite IE. Of these, 14 (15.2%) had spondylodiscitis. The mean age of patients with spondylodiscitis was 69.1±13.6 years (range, 33–87 years). The main clinical features are reported in Table 1. Predisposing heart disease was found in nine (64.3%) cases (Table 2).

All patients complained of back pain: lumbar pain in 10 (71.4%) cases, dorsal pain in 3 (21.4%) cases, and cervical pain in 1 (7.2%) case. The diagnosis of spondylodiscitis was always established before the diagnosis of IE except in one patient in whom both diagnoses were established simultaneously. The mean delay between diagnosis of spondylodiscitis and diagnosis of IE was 22.6 days (range, 0–80 days). To confirm spondylodiscitis, magnetic resonance imaging was used in seven cases and computed tomography (CT) in six cases. In one case CT scan imaging could not be performed, and the diagnosis was suggested by bone scintigraphy and confirmed by puncture of the intervertebral disk space.

The localization of valve involvement is detailed in Table 2. Laboratory data are shown in Table 3. Inflammatory syndrome was present in all cases. Table 4 lists the organisms isolated from blood cultures; all organisms were gram-positive cocci. Data concerning the outcome of IE are shown in Table 5. Two patients developed congestive heart failure, one of whom died. Overall mortality was 14.3%.

Upon comparing the two groups of patients without (group 1) and with spondylodiscitis (group 2), it was found that age, gender, and previously known underlying diseases were not relevant (Table 2). Nevertheless, patients with IE and spondylodiscitis were more often over 60 years of age (85.7% vs. 57%, *P*=0.09). When we combined patients with artificial heart valves and patients with pacemakers, we found a significantly higher proportion of patients in group 2 (64.3%) (*P*=0.04).

No differences between groups were found in clinical features or laboratory values (Table 3). Differences between the two groups with regard to organisms isolated from blood are shown in Table 4. Of the 20 patients with

Table 3 Comparison of clinical and laboratory values in group 1 patients (those with infective endocarditis not associated with spondylodiscitis) versus group 2 patients (those with infective endocarditis and spondylodiscitis)

CRP, C-reactive protein; NS, nonsignificant

	Group 1 (*n*=78)	Group 2 (*n*=14)	*P* value
No. with fever (temperature >38°C)	62 (79.5%)	10 (71.4%)	NS
No. with microhaematuria	67 (86%)	12 (85%)	NS
No. with elevated liver enzymes	24 (31%)	2 (12%)	NS
Mean haemoglobin value in g/dl ±SD (range)	11.4±2.1 (7.7–16.5)	10.8±1.7 (7.8–13.7)	NS
No. with leukocytosis (>11,000/mm^3)	32 (44.4%)	7 (50%)	NS
Mean CRP in mg/l ±SD (range)	91.6±78.7 (12–347)	87.6±49.6 (20–171)	NS
Mean sedimentation rate in mm/h ±SD (range)	71.5±34.7 (11–140)	74.6±26.4 (35–113)	NS

Table 4 Causative organisms cultured from blood in 92 patients with infective endocarditis: 78 without spondylodiscitis (group 1) and 14 with spondylodiscitis (group 2)

CNS, coagulase-negative staphylococci; NS, nonsignificant

Causative organism	Group 1 (*n*=78)	Group 2 (*n*=14)	*P* value
Streptococci	15 (19.2%)	3 (21.4%)	NS
Staphylococci	32 (41%)	6 (42.9%)	NS
S. aureus	16 (20.5%)	2 (14.3%)	NS
CNS	16 (20.5%)	4 (28.6%)	NS
Group D streptococci	22 (28.2%)	5 (35.7%)	NS
Gram-negative bacilli	6 (7.7%)	0	NS
None	1 (1.3%)	0	NS
Other	2 (2.6%)	0	NS

Table 5 Outcome in the 98 patients with infective endocarditis: 78 without spondylodiscitis (group 1) and 14 with spondylodiscitis (group 2)

NS, nonsignificant

Parameter	Group 1 (*n*=78)	Group 2 (*n*=14)	*P* value
Delay to apyrexia in days [mean ±SD (range)]	6.2±5.8 (0–30)	8.3±6 (0–21)	NS
Length of treatment in days [mean ±SD (range)]	44.5±14.7 (21–90)	147.6±40.5 (56–210)	<0.01
Length of hospitalization in days [mean ±SD (range)]	47.9±23.2 (17–140)	73.4±48.8 (34–210)	0.005
Favorable outcome [no. (%)]	62 (79.5)	12 (85.7)	NS
Cardiac surgery [no. (%)]	38 (48.7)	8 (57.1)	0.08
Death [no. (%)]	12 (15.4)	1 (7.1)	NS

IE caused by coagulase-negative staphylococci, only four had no intracardiac device, all of whom belonged to group 1.

The delay to apyrexia was similar in the two groups, but both the length of hospitalization and the length of treatment were, as expected, significantly longer in the group of patients with spondylodiscitis (P=0.005 vs. P<0.001, respectively). Nevertheless, the duration of intravenous antibiotic treatment was the same in the two groups.

The proportion of patients still alive after 1 year of follow-up was 93% (13/14) in group 2 and 83.5% (60/72) in group 1 (P>0.05) (Table 5). Cardiac surgery was performed in 39 (49.4%) patients in group 1 and in 8 (61.5%) patients in group 2.

Discussion

In the present study, the prevalence of spondylodiscitis in patients with IE was 15%. Many studies have emphasized the common occurrence of rheumatic manifestations in patients with IE [1, 3, 7]. Spondylodiscitis, however, has rarely been described, and then usually only in case reports [9, 10, 11, 12, 13]. Ninet et al. [14] found the prevalence of spondylodiscitis in patients with IE to be 5.9%, whereas Thomas et al. [2] reported a prevalence of 3.7% among 108 patients with IE and Morelli et al. [9] three cases in a series of 30 patients. These studies included patients with a possible diagnosis of IE according to the Duke criteria.

The apparent rarity of spondylodiscitis in association with IE contrasts with the high frequency of back pain in patients with IE. In most studies of IE, back pain was present in up to 43% of the patients [6]. Many mechanisms have been suggested in the pathogenesis of these symptoms, such as bacterial emboli or immune dysfunction [2, 5, 6, 15]. We wonder whether the initial back pain could also be explained by early spondylodiscitis that is not rapidly cured by the antibiotics prescribed for IE. In our study, the high prevalence of spondylodiscitis associated with IE is probably related to the considerable delay between the diagnosis of IE and the diagnosis of spondylodiscitis. This hypothesis is strengthened by the fact that, in the majority of cases, spondylodiscitis arises from haematogenous dissemination.

Many features of our patients with spondylodiscitis and IE are similar to those described in previously pub-

lished reports [13, 14, 16], notably age (patient >55 years) and gender (male predominance). However, we did not find any differences between the two groups of patients. The symptoms were also similar to those described in previous cases, including cases of spondylodiscitis alone [17, 18]. Localized pain was always present and antedated the diagnosis of IE by many days (more than 22 days in our series). The lumbar region is most commonly involved, but an unusual finding on the cervical spine has also been reported [10]. Other series of patients with spondylodiscitis reported no difference between patients with spondylodiscitis alone and those with spondylodiscitis and IE, although the prognosis was poorer in patients with IE [16, 19].

A wide variety of bacteria are found in cases of IE associated with spondylodiscitis, such as *Rothia dentocariosa*, *Pasteurella dagmatis*, and *Propionibacterium acnes* [20, 21, 22]. However, in most cases, as in our study, group D *Streptococcus* is the most frequent causative organism [10, 14]. Coagulase-negative staphylococci are also frequently isolated. The role of a pacemaker in infection caused by coagulase-negative staphylococci has been demonstrated. Recently, Bucher et al. [11] reported three cases of spondylodiscitis caused by coagulase-negative staphylococci, one of which was associated with IE. In a prospective study of IE in patients with pacemakers, Klug et al. [23] found that *Staphylococcus epidermidis* caused 75% of the cases of subacute endocarditis, and the presentation was mostly (75%) chronic. The long delay before the diagnosis of IE due to coagulase-negative staphylococci in patients with a pacemaker might explain the development of spondylodiscitis during persistent bacteremia [12].

Except for duration of treatment and hospitalization, we did not find any significant differences between IE alone and IE with spondylodiscitis, especially with regard to patient age and gender, clinical and laboratory features, and evolution of disease. The prolonged treatment of patients in group 2 can be explained by the lengthy treatment of spondylodiscitis, which can range from 6 weeks to 3 months according to previous reports [24, 25]. The duration of treatment for IE, on the other hand, ranges between 2 and 6 weeks, depending on the causative bacteria. However, we found no difference between the groups in the IE treatment regimen. Heart valve replacement seemed to be more frequent in the group with spondylodiscitis. This association constitutes an argument for considering spondylodiscitis as a complication of IE. The fact that endocardial lesions are more often located at the aortic valve (43%) lends support to this hypothesis and indicates that spondylodiscitis is probably secondary to persistent bacteremia during IE. The analysis of this data and of the other series reported in the literature [14] suggests that the occurrence of spondylodiscitis in a patient with IE does not worsen the patient's prognosis. Rather, the outcome depends mainly on the severity of IE.

We acknowledge several limitations of our study. First, ours is a retrospective study, and some data are missing, especially concerning the presence of back pain. Nevertheless, we believe that the prevalence of spondylodiscitis found was below the true rate due to the retrospective nature of this study. Second, it would be interesting to have, for all patients with a diagnosis of IE who report back pain, an imaging technique (for example, magnetic nuclear resonance) to search for associated spondylodiscitis. Despite these limitations, our study provides the first analysis of spondylodiscitis in the setting of IE using the Duke criteria.

Our results suggest that a frequent association between IE and spondylodiscitis exists and may have some implications. The diagnosis of spondylodiscitis alone always antedates that of IE and spondylodiscitis together. Moreover, a high percentage of patients with IE have associated spondylodiscitis. Consequently, echocardiography should be routinely performed in all patients with spondylodiscitis. The therapeutic management of IE often requires surgery [9].

In conclusion, the mechanisms of the pathogenesis of spondylodiscitis are still unexplained and are attributed to microemboli or bacteremia. However, this study shows that the occurrence of spondylodiscitis in association with IE is not rare. This finding poses a major concern for patients with spondylodiscitis who have risk factors for IE. Practitioners should be particularly aware of back pain when IE is diagnosed so that the possibility of associated spondylodiscitis is not underestimated.

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