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Spondylodiscitis due to *Propionibacterium acnes*: report of twenty-nine cases and a review of the literature

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Abstract

Propionibacterium acnes is the most frequent anaerobic pathogen found in spondylodiscitis. A documented case required microbiological proof of *P. acnes* with clinical and radiological confirmation of inflammation in a localized region of the spine. Microbiological samplings were obtained by surgery or aspiration under radiological control. Twelve males and 17 females (median age, 42 years) with spondylodiscitis due to *P. acnes* were diagnosed within the last 15 years. Three patients were immunosuppressed. All patients reported back pain as the main symptom, and most were afebrile. Three patients had a peripheral neurological deficit, one a motor deficit, and two a sensory deficit attributable to the infection; and six patients had an epidural abscess. The most frequent risk factor was surgery, which was present in the history 28 of 29 (97%) patients. The mean delay between spinal surgery and onset of disease was 34 months, with a wide range of 0–156 months. Osteosynthesis material was present in twenty-two cases (76%). In 24 (83%) patients, additional surgery, such as débridement or spondylodesis, was performed. Previous osteosynthesis material was removed in 17 of the 22 (77%) patients where it was present. Total cure was reported in all patients, except one, after a mean duration of antibiotic therapy of 10.5 weeks (range, 2–28 weeks). In conclusion, spondylodiscitis due to *P. acnes* is an acute infection closely related to previous surgery. The most prominent clinical feature is pain, whereas fever is rare, and the prognosis is very good.

Keywords: Anaerobes, case series, *Propionibacterium acnes*, spondylodiscitis
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Introduction

Spondylodiscitis, together with septic discitis, vertebral osteomyelitis and epidural abscess, accounts for 2–7% of all cases of osteomyelitis [1,2]. The incidence of postoperative infection is in the range 0–3% [3] or 0.7–0.8% with adequate antibiotic prophylaxis [4]. Treatment of spondylodiscitis usually requires an invasive diagnostic approach and long-lasting antibiotic therapy, occasionally associated with surgical intervention [1,2]. Prolonged hospital stay is often unavoidable and comprises a major contributor to increased cost. The most prevalent pathogens are *Staphylococcus aureus* and other aerobic Gram-positive organisms [1,3–5]. In industrialized countries, only a minority of cases are due to Gram-negative aerobic organisms, tuberculosis, fungi, parasites [6] or anaerobes [2,7]. Indeed, anaerobic disease is very rare and a retrospective review of 253 cases of spondylodiscitis revealed only two (0.8%) due to anaerobic bacteria [8]. These cases are mostly seen in postoperative, rather than in non-operative, cases (17.4% vs. 5.1%) [9].

Propionibacterium acnes is a microaerophilic anaerobic, Gram-positive rod [10] isolated from a wide variety of infections and usually found on the skin. The traditional view that *P. acnes* is nonpathogenic for man, except in acne vulgaris,

should be abandoned. The proportion of reported bone infections caused by *P. acnes* varies in the range 2.8–12% [11]. In the present study, we analysed all cases of spondylodiscitis due to *P. acnes* in seven tertiary hospitals, comparing risk factors, treatment and clinical outcomes with the reports available in the literature.

Materials and Methods

Settings

This retrospective review was conducted in seven hospitals, including the University Hospital of Geneva (Switzerland) and six university hospitals in France (Garches, Nantes, Rennes, Angoulême, Besançon and Tours). All cases of microbiologically documented spondylodiscitis due to *P. acnes* as of May 2007 were retrieved from medical and laboratory records.

Case definition and parameters

The case definition required microbiological proof of *P. acnes*, clinical evidence of infection, and radiological confirmation of inflammation in a localized area of the spine. The patient must not have been under antibiotic treatment. Microbiological documentation required at least two different isolates of the same *P. acnes* strain from intra-operative tissue specimens and/or abscess aspiration under radiological control. *Propionibacterium acnes* must have been the predominant pathogen in all cultures that additionally showed an elevated number of leukocytes as a hallmark of inflammation. The presence of co-pathogens in one single sample did not exclude the impact of *P. acnes* retrieved in several samples. Each contributing centre used its own established protocols for aerobic and anaerobic cultures, which were not changed for the present study. *Propionibacterium* sp. other than *P. acnes* were excluded.

Clinical parameters and cure rates

Descriptive statistics were used to assess the prevalence of various clinical and laboratory parameters associated with individual *P. acnes* spondylodiscitis (Table 1). Cure was defined as an absence of clinical, biological and radiological evidence of infection.

Results

Twelve males and 17 females with a median age of 42 years (range, 14–78 years) were identified within the last 15 years. All patients were immunocompetent except three: one patient with non-insulin dependent diabetes, one on steroid medication, and one patient with HIV. Only one patient had concomitant inflammation elsewhere, and this was a male with chronic prostatitis. No patient had pathology in the oral cavity, the gastrointestinal tract, or on the skin. The most frequent risk factor was surgery, present in the history of 28 of 29 (97%) patients, with osteosynthesis material present in 22 (76%) patients. The mean delay between spinal surgery and onset of disease was 34 months (range, 0–156 months). The median time to diagnosis was 4.7 months (range, 1 week to 104 weeks).

All patients reported back pain as the main symptom, and most were afebrile. The affected vertebral regions were thoracic in 14 cases, lumbar in 13 cases, and thoraco-lumbar in two cases. Three patients had a peripheral neurological deficit, one had a motor deficit, and two had a sensory deficit attributable to the infection; and six patients had an epidural abscess (Fig. 1). A total leukocyte count >6 Giga/L was present in 16 (56%) patients, and the mean C-reactive protein. level was 31.7 mg/dL (range, 0.36–118 mg/dL), both prior to eventual débridement. Blood cultures were not performed for 13 patients. Blood cultures were negative for *P. acnes* in the remaining patients, except for one. The incubation time of the blood culture bottles was unknown.

In eight cases, the predominant *P. acnes* was associated with other pathogens, including coagulase-negative *Staphylococcus* (n = 4), *Lactobacillus* sp (n = 1), *Pseudomonas aeruginosa* (n = 1), *Enterococcus* (n = 1) and *Streptococcus* of Lancefield group F (n = 1). β-lactam antibiotics were the most frequently used antimicrobial agent (15/29 patients). Among the oral medications, fluoroquinolones were preferred. Only eight patients received a single antimicrobial agent throughout the entire course of treatment. In 24 (83%) patients, additional surgery, such as débridement or spondylodesis, was performed. Previous osteosynthesis material was removed in 17 of the 22 (77%) patients where it was present.

The mean follow-up period was 18 months (range, 4 months to 7 years). Total cure was reported in all patients, except one, after a mean duration of antibiotic therapy of 10.5 weeks (range, 2–28 weeks). The mean duration of hospitalization was 18 days (range, 4–63 days).

Discussion

Propionibacterium acnes spondylodiscitis is rare. To our knowledge, the cohort of 29 patients involved in the present study constitutes the largest case series of spondylodiscitis due to *P. acnes*. As with every skin commensal, wound contamination may lead to false-positive microbiological findings. Carricajo *et al.* [12] reported that 18.5% of patients

TABLE 1. **Spondylodiscitis due to *Propionibacterium acnes*: reports in the literature and the present study cases**

References	No. cases	Gender	Age (years)	Risk factor	Delay between surgery and onset of disease (weeks)	Additional surgery	Antibiotic therapy	Duration of antibiotic therapy (weeks)	Outcome (cure)
Newman [14]	1	M	75	No	4	No	Penicillin G	15	Yes
Serushan [15]	1	M	27	Steroids	12	No	Penicillin G	6	Yes
Noble [16]	1	M	50	Discectomy	4	No	Penicillin G	8	Yes
Suter [17]	1	F	23	Not mentioned	16	No	Rifampicin & cotrimoxazol	9	Yes
Gerster [18]	1	F	45	Psoriasis	Not mentioned	No	Amoxicillin–clavulanate	6	Yes
Abolnik [19]	1	F	43	Lumbar puncture	36	Yes	Clindamycin	6	Yes
Jakab [25]	3	M	60	Not mentioned	Not mentioned	Yes	Not mentioned	6.5	Not mentioned
		M	64	Discectomy	3	Yes	Not mentioned	6	Not mentioned
		M	60	Discectomy	9	Yes	Not mentioned	6	Not mentioned
Chia [26]	4	M	33	Discectomy	2	No	Penicillin G	6	Yes
		M	65	Epidural catheter D	10	No	Penicillin G & clindamycin	6	Yes
		F	24	Discectomy	105	No	Penicillin G	5	Yes
		M	46	Discectomy	3	No	Penicillin G + Clindamycin	6	Yes
Crouzet [27]	2	M	55	No	Not mentioned	No	Ofloxacin + Amoxicilline–clavulanate	7	Yes
		M	31	IV drug abuse?	26	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Hammann [20]	1	F	51	Epidural catheter	6	No	Penicillin G & clindamycin	3	Yes
Corpataux [21]	1	F	51	Epidural catheter	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Hustache [28]	2	F	48	Foramenotomy	4	No	Oxacillin & ciprofloxacin	6	Yes
		M	39	No	Not mentioned	No	Pristinamycine & ciprofloxacine	6	Yes
Retornaz [22]	1	M	35	Discectomy	3	No	Ciprofloxacin & clindamycin	8	Yes
Hernandez [23]	1	F	34	Lumbar puncture	3	No	Ciprofloxacin	6	Yes
Harris [24]	1	M	64	Discectomy	7	Yes	Penicillin G	8	Yes
Current study series	29	12 M, 17 F	42	Implant present: 22 Others: 6	Mean: 136 weeks Range: 0–624	Yes: 24/29 cases	Amoxicillin & fluoroquinolones	Mean: 10.5 weeks Range: 2–28	Yes: 28/29 cases
Global analysis	*n* = 51	26 M, 25 F	Mean: 44 years Range: 14–78	Previous invasive procedure in 84%: surgical material: 22 discectomy: 10 epidural catheter: 3 lumbar puncture: 2 foramenectomy: 1 other interventions: 4	Mean: 89 weeks Range: 0–624	Yes: in 29 of 51 cases (59%)	Monotherapy: 37% Combination therapy: 63%	Mean: 8.7 weeks Range: 2–28	Cure in 98%

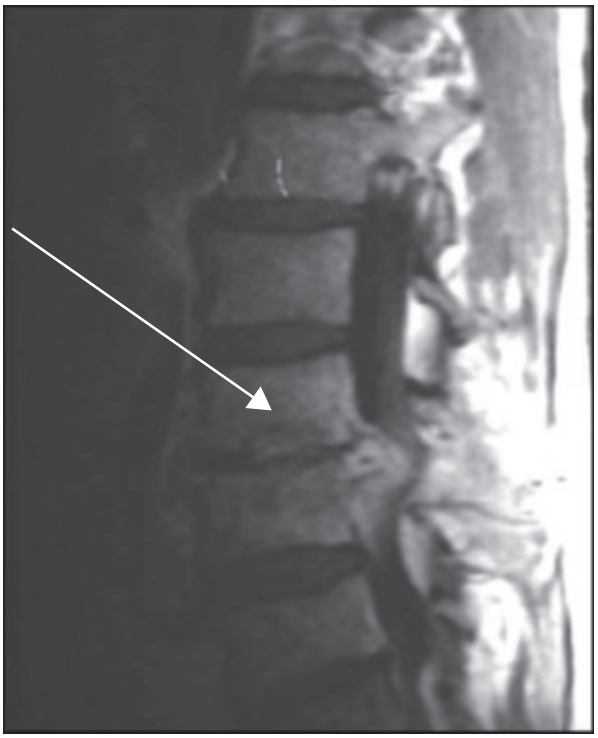

FIG. 1 Epidural abscess in spondylodiscitis due to *Propionibacterium acnes*.

undergoing surgery for lumbar disk herniation revealed the presence of *P. acnes* in intra-operative specimens. However, this was an outbreak situation linked to contaminated laminar airflow in the operating theatre [12]. McLorinan *et al.* [13] demonstrated wound contamination due to *P. acnes* and staphylococci in uninfected patients who underwent spinal surgery. It was unusual in their study that skin samples without underlying osteosynthesis material were vortexed and exposed to ultrasonification [13], which are procedures likely to enhance a microbiological result for skin commensals. By contrast, patients in the present study were all infected; intra-operative specimens showed clear-cut inflammation with the presence of *P. acnes* in several specimens, and the absence of an alternative predominant pathogen. Hence, we have no doubt about the diagnosis of a true infection in the present study.

The present review of the literature resulted in 15 reports concerning spondylodiscitis due to *P. acnes*, which, along with our own cases, are summarized in Table 1. Eleven articles were case reports [14–24] and five were case series [25–29], of which the largest involved four patients [26]. An additional report [29] revealed insufficient information.

Most findings of *P. acnes* spondylodiscitis were consistent with reports of aerobic spondylodiscitis, but differed in some aspects. First, although spondylodiscitis can occur in children, it is primarily a disease of the fifth or sixth decade of life [30], and the median age of all patients in Table 1 was 44 years, which is lower than that reported in cases of aerobic disease with mean ages of 61 [31], 59 [1] or 64 years [32], Second, only six patients in the present series had an epidural abscess, which is a common feature in aerobic disease [5,9]. For all of the patients listed in Table 1 (reports in the literature and present study), the mean delay between a previous invasive procedure and disease was 89 weeks (range, 0–624 weeks), which is very close to the incubation period, and was clearly longer than the average of 4 [9] or 7 weeks [8] reported for aerobic cases.

The median time to diagnosis of 4.7 months (range, 1 week to 24 months) was clearly longer than the average of 2.5 months [8] for aerobic cases.

In the present study, differences from other anaerobic pathogens of spondlyodiscitis were also observed. Fever was usually absent, unlike a retrospective report of non-*P. acnes* anaerobic spondylodiscitis where fever was reported in 40% of those affected [2]. Blood cultures were negative for all but one patient in this series. In other reports, blood cultures were positive in 15% of cases of anaerobic spondylodiscitis [2], and 21% [8] or 56% [9] of cases of aerobic disease.

The site of infection among the present patients was equally divided between the thoracic and lumbar spine, which differs from other reports of anaerobic [2] or aerobic spinal infections [1,8,31] where lumbar localization predominated.

The degree to which the reported clinical description is a consequence of *P. acnes* itself or whether it would be true of any aerobic skin organisms introduced during surgery is unclear.

The characteristics of postoperative spondylodiscitis may be similar to those presented in the present study [9,33], although differences exist. The prolonged delay in arriving at the correct diagnosis, the prolonged incubation time for microbiological cultures [34], the high sensitivity to penicillin [35], and the prolonged delay between surgical procedure and infection highlight some of the key differences between *P. acnes* and its aerobic counterparts.

The frequent risk factors for anaerobic disease include poor oral hygiene, dental procedures, and bites [2,7]. In a study of bacteraemia after endodontic procedures, samples from the root canal of 26 subjects revealed anaerobic bacteria. Blood cultures were positive for the same organism in 11 of these subjects [36]. The pathogenesis of *P. acnes* spondylodiscitis infection appears to be different. We found a strong causal correlation between *P. acnes* infection and previous invasive procedures in 97% of patients, whereas 'spontaneous' infection has been reported to occur more frequently with other anaerobes [2] or aero-

bic pathogens [1,5,8,9,29]. Similar to our results, Nisbet *et al.* [35] reported a post-craniotomy prevalence of 96% in their neurosurgical patient population. The affinity for surgical site infections can be explained by the nature of *P. acnes*. Its microaerophilic character enables it to live on skin and in sebaceous glands [10]. *Propionibacterium acnes* can tolerate up to 100% oxygen [37] and is capable of surviving up to 8 months under anaerobic conditions *in vitro*, suggesting that it could also survive in human tissue with low oxidation potential, such as the vertebral disk [38]. Finally, it resists phagocytosis and can persist intracellularly within macrophages [30]. Therefore, it is not surprising that *P. acnes* infection correlates strongly with invasive procedures such as neurosurgery [35], lumbar puncture [19–21,23] and orthopaedic surgery [34]. Postoperative septic arthritis of the shoulder due to *P. acnes* may become an emerging clinical entity [34].

For spondylodiscitis in general, there are no randomized or prospective studies concerning the optimal choice and duration of antibiotic treatment, as well as the role of surgery [32]. In many patients (Table 1), an additional surgical intervention such as debridement, spondylodesis or removal of osteosynthesis material, was necessary. This correlates with the reports concerning aerobic spondylodiscitis [8,9]. In the past, *P. acnes* was usually sensitive to many antibiotics, but the emergence of antibiotic resistance in *P. acnes*, and the danger of propagation of untreated disease to the epidural space with subsequent high morbidity and mortality [5], necessitates the testing of isolated strains [30,39]. Intravenous penicillin G and amoxicillin are the most frequently prescribed antibiotics [35,40], followed by oral clindamycin or fluoroquinolones. Clindamycin is an appropriate oral treatment with excellent bone-to-serum ratio, whereas β-lactams have an inferior ratio [41]. By contrast to other anaerobes, *P. acnes* is naturally resistant to metronidazole [19,39,42].

The duration of antibiotic treatment is often based on past experience with aerobic pathogens [1,5], although several reports describe anaerobic spondylodiscitis as being less virulent, with a better prognosis than its aerobic counterpart [2,25].

The minimal duration of *P. acnes* infection may be 6 weeks, and we do not believe that it can be shortened as is implied by the case of the one patient referred to in Table 1 [20] or a single retrospective study of intracranial infections [35]. With the high likelihood of additional surgical intervention for spondylodiscitis [1,2,8], and the slow growth characteristics of *P. acnes* [9,11,22,25,27,34], a shorter duration of antibiotic therapy should not be attempted without controlled studies and/or concomitant debridement. However, initial oral treatment should be possible, even if this approach is not currently supported by randomized trials. Prevention of infection after spinal surgery remains of utmost importance [3,43,44] and, fortunately, the usual antibiotics for preoperative prophylaxis cover *P. acnes*.

Cure was achieved in every patient in this series except one, in contrast to cases of aerobic spondylodiscitis, where 50% of patients were reported to have complaints at follow-up [3,31]. Mann *et al.* [45] reported sequelae in 55% of patients. McHenry *et al.*[8] reported persistent disability in more than 33% of patients, relapse in 14%, and death in 11%. This difference may be a result of the younger age of patients with postoperative infection due to *P. acnes* [9], which correlates with the absence of co-morbidities among this population, another hallmark of 'spontaneous' spondylodiscitis [1,9,29]. In the present patient group, neurological deficits attributable to the infection were present in only three (10%) patients. In other reports of patients with anaerobic [2] or aerobic disease, neurological deficit has been reported in 27% [1], 39% [9] and even >50% [45] of patients.

In conclusion, spondylodiscitis due to *P. acnes* is strongly related to previous intervention, and prevention remains critical. The longer incubation period must be taken into account with respect to microbiological cultures. The prognosis appears excellent. The therapeutic approach is not standardized, but antibiotic treatment is usually prescribed for 6 weeks and often complemented by surgery. Penicillin G, amoxicillin and clindamycin have proven their efficacy in effecting a cure. As a result of the rarity of spondylodiscitis due to *P. acnes*, only large comparative prospective studies will be able to address epidemiology and optimal therapy.

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Transparency Declaration

All authors declare that they have no commercial or other association that might pose a conflict of interest.

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