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【 CASE REPORT 】

Spontaneous Pyogenic Spondylitis and Possible Infective Endocarditis Caused by *Aggregatibacter actinomycetemcomitans*

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Abstract:

Aggregatibacter actinomycetemcomitans, an etiological agent associated with periodontitis, endocarditis, and other infections, has rarely been implicated in spondylitis. A 70-year-old man with aortic valve replacement presented with a 4-month history of lower back pain and was diagnosed with spondylitis. Prolonged incubation of blood cultures and a biopsy yielded *A. actinomycetemcomitans*. Concurrent infective endocarditis (IE) was probable considering the infectious organism and the patients' prosthetic valve. The patient was treated with ceftriaxone and recovered well. Pyogenic spondylitis with possible concurrent IE may be caused by *A. actinomycetemcomitans*. Extended incubation and repeated cultures should be considered if *Haemophilus* spp., *Aggregatibacter* spp, *Cardiobacterium* spp, *Eikenella* spp, and *Kingella* spp. (HACEK) infection is suspected.

Key words: *Aggregatibacter actinomycetemcomitans*, pyogenic spondylitis, infective endocarditis

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Introduction

Aggregatibacter actinomycetemcomitans belongs to the HACEK (*Haemophilus* spp., *Aggregatibacter* spp, *Cardiobacterium* spp, *Eikenella* spp, and *Kingella* spp.) group of bacteria, which are commensal microbiota that colonize the oral-pharyngeal region in humans. The pathobiont *A. actinomycetemcomitans* has been implicated in periodontitis, endocarditis, and other infections (1); however, its association with pyogenic spondylitis has rarely been reported.

We herein report a rare case in which *A. actinomycetemcomitans* infection developed concurrently with pyogenic spondylitis and possible infective endocarditis (IE), as diagnosed by the modified Duke Criteria (2).

Case Report

A 70-year-old man with a history of aortic regurgitation that had been treated with aortic valve replacement at 62 years old presented to the emergency department with lower back pain. He had a four-month history of pain prior to presentation. Previously, he had visited another hospital and been treated with analgesics, which provided mild, short-term symptomatic relief. In the absence of a specific diagnosis, the patient continued to experience pain in the proceeding months but was not marked by a fever, chills, or night sweats. Three weeks before admission, he was brought to our hospital by ambulance with recurring back pain, treated with diclofenac, and discharged. However, the patient was readmitted to our hospital as the chronic pain increased in severity and he became unable to walk or stand.

Upon presentation, the patient was alert, and his vital signs were as follows: temperature of 35.8℃, blood pressure of 107/69 mmHg, regular heart rate of 70 beats/min, and respiratory rate of 16 breaths/min. A physical examination revealed anemic conjunctiva, periodontitis, mechanical valve sounds, systolic murmur at apex, and L4-L5 tenderness. No

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Table 1. Laboratory Data on Admission.

CBC		Chemistry		Urinalysis	
WBC	11,190 /μL	TP	7.7 g/dL	SG	1.020
Neut	84.0 %	Alb	2.8 g/dL	pH	5.5
Lym	9.0 %	AST	15 IU/L	Prot	+/-
Mono	6.0 %	ALT	16 IU/L	Glu	-
Eosi	0.0 %	LDH	192 IU/L	Uro	+/-
Baso	1.0 %	BUN	27 mg/dL	Bil	-
RBC	270 *10^4/μL	Cr	1.05 mg/dL	Ket	-
Hb	8.0 g/dL	Na	136 mEq/L	Bld	2+
Ht	24.2 %	K	4.6 mEq/L	WBC	-
MCV	89.6 fL	Cl	106 mEq/L		
MCH	29.6 pg	CRP	12.3 mg/dL		
PLT	43.1 *10^4/μL	ESR	134 mm/h		

Alb: albumin, ALT: alanine aminotransferase, AST: aspartate aminotransferase, Baso: basophil, Bil: bilirubin, Bld: blood, BUN: blood urea nitrogen, CBC: complete blood count, Cl: chlorine, Cr: creatinine, CRP: C-reactive protein, Eosi: eosinophil, ESR: erythrocyte sedimentation rate, Glu: glucose, Hb: hemoglobin, Ht: hematocrit, K: potassium, Ket: ketone, LDH: lactate dehydrogenase, Lym: lymphocyte, MCH: mean corpuscular hemoglobin, MCV: mean corpuscular volume, Mono: monocyte, Na: sodium, Neut: neutrophil, PLT: platelet, Prot: protein, RBC: red blood cell, SG: specific gravity, TP: total protein, Uro: urobilinogen, WBC: white blood cell

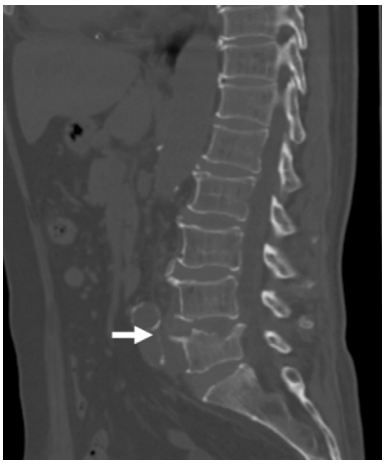

Figure 1. A CT image of the lumbar spine shows an irregular erosion of the superior end plate of the L5 vertebra (arrow) and a possible fluid collection in the intervening L4/L5 disc space. Abscess formation is not detected. CT: computed tomography

skin lesions or neurological symptoms were noted. Extensive periodontitis was confirmed by a dentist. Laboratory tests showed a white blood cell (WBC) count of 11,190/μL with 84% neutrophils, hemoglobin concentration of 8.0 g/dL, C-reactive protein (CRP) of 12.3 mg/dL, and an erythrocyte sedimentation rate (ESR) of 134 mm/h. Other results are shown in Table 1. His chest X-ray and electrocardiogram findings were unremarkable.

Computed tomography (CT) of his lumbar spine showed L5 end plate erosion (Fig. 1). No abscess formation was detected. Magnetic resonance imaging (MRI) revealed T1-weighted low-intensity and T2-weighted high-intensity regions at the L4-L5 disc (Fig. 2A, B). This region showed a high signal intensity on short tau inversion recovery (STIR) imaging (Fig. 2C). The radiographic findings were suggestive of spondylitis of the L4-L5 spinal segment, and a CT-guided needle biopsy was performed on hospital day 5. Empiric antibiotic therapy with ceftriaxone (2 g intravenously daily) and vancomycin (target trough level of 15 to 20 μg/mL) was administered after the biopsy.

The biopsy specimen subsequently yielded *A. actinomycetemcomitans*, which was also isolated from blood cultures obtained on admission and hospital day 5 (Fig. 3). Blood cultures required a prolonged incubation period of four days to more than one week before growth was detected and several more days to identify the organism. The culture of the biopsy specimen was positive on hospital day 13, and the organism was identified on hospital day 15. Antibiotic monotherapy was changed to ceftriaxone (2 g intravenously daily) based on an antimicrobial susceptibility test (Table 2). Since *A. actinomycetemcomitans* often causes endocarditis, transesophageal echocardiography (TEE) was performed, and neither vegetation nor destruction of valves were detected. Head MRI did not reveal findings suggestive of infectious lesions or a cerebral infarction. We also considered positron emission tomography (PET)-CT for the prosthetic valve endocarditis assessment but did not ultimately perform it because it was not covered by insurance.

Antibiotic therapy was continued for eight weeks after a negative blood culture was confirmed. This was in accordance with pyogenic spondylitis and IE treatment guidelines, which recommend six to eight weeks of antibiotic therapy (3-7). The patient responded well to treatment, and his

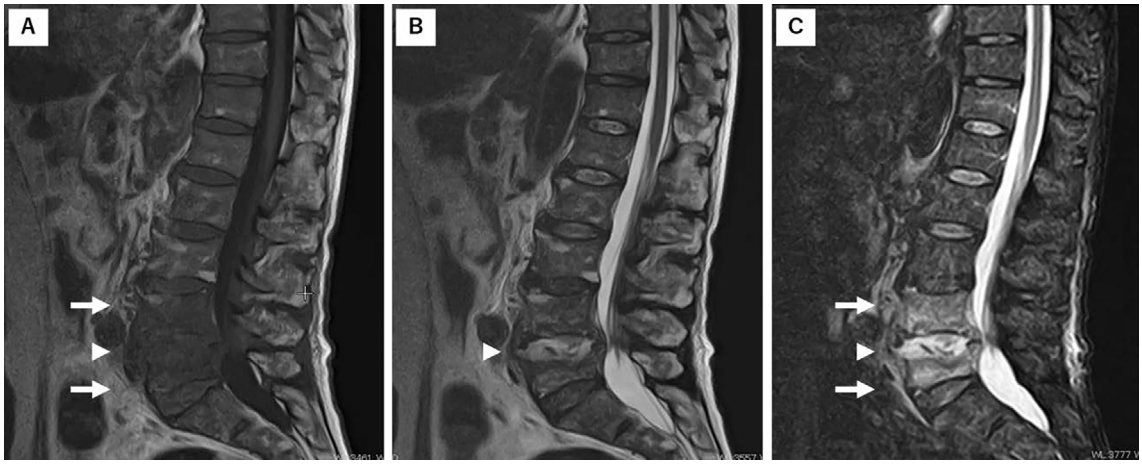

Figure 2. **MRI of the lumbar spine. (A) T1-weighted image shows decreased signal intensity in the L4 and L5 vertebral bodies (arrows) and loss of end plate definition (arrow head). (B) T2-weighted image demonstrates increased signal in the L4/L5 interval disc space (arrow head). (C) Short tau inversion recovery image shows increased signal in the intervertebral disc space (arrow head) and adjacent L4 and L5 vertebral bodies (arrows). MRI: magnetic resonance imaging**

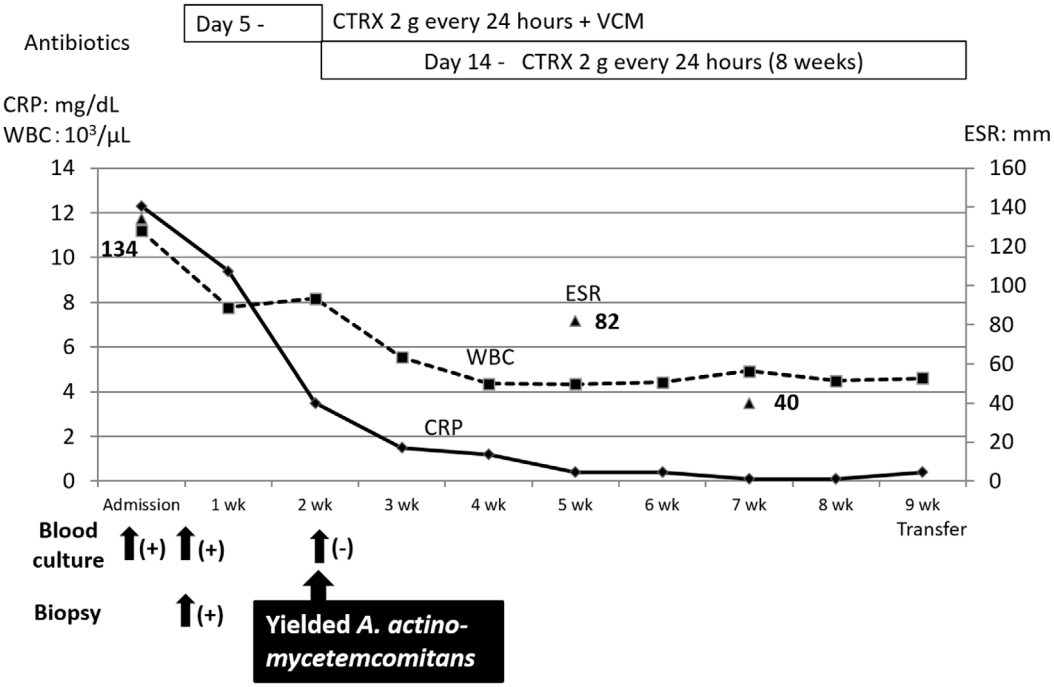

Figure 3. **Clinical course of the patient. Blood cultures were obtained on admission and hospital day 5, both of which were positive, with the organism identified as *A. actinomycetemcomitans* after a prolonged incubation period. A biopsy performed on hospital day 5 also yielded the same result. A follow-up culture obtained on day 14 was confirmed negative, and antibiotic therapy was continued for another eight weeks. The WBC, CRP, and ESR values showed marked declines after the antibiotic therapy was started. CRP: C-reactive protein, CTRX: ceftriaxone, ESR: erythrocyte sedimentation rate, VCM: vancomycin, WBC: white blood cell, wk: week**

lower back pain was resolved. The CRP levels (0.09 mg/dL) and ESR (40 mm/h) were markedly reduced after 5 weeks of antibiotic therapy. The patient was transferred to another hospital to continue antibiotic therapy and rehabilitation after 63 days of admission. There was no evidence of infection or pain recurrence in the 12-month follow-up period.

Discussion

This report indicated that a patient with the insidious onset of back pain and a history of heart valve replacement and extensive dental disease concurrently developed pyo-

genic spondylitis and possible IE caused by *A. actinomycetemcomitans*. Extended incubation and repeated blood cultures led to the detection and identification of the pathogenic organism.

Three important clinical issues were noted from the clinical course of this patient: 1) *A. actinomycetemcomitans* may cause pyogenic spondylitis, 2) Concurrent IE may have been present in this *A. actinomycetemcomitans*-mediated spondylitis case, and 3) Infection was caused by *A. actinomycetemcomitans*.

First, to our knowledge, only five cases of pyogenic spondylitis caused by *A. actinomycetemcomitans* have been reported (8-12) (Table 3). This limited number of reports may suggest a low frequency of infections. However, there may be some unrecognized *A. actinomycetemcomitans* spondylitis cases. A systematic review of 14 studies including 1,008 patients with pyogenic spondylitis reported that the yield of blood culture was 30-78%, while a CT-guided needle biopsy or open biopsy provided a yield of 47-100%, and overall, the causative organism of pyogenic spondylitis was unknown in up to 33% of cases (13). Slow growth of *A. actinomycetemcomitans* is observed in standard culture media, and isolation requires prolonged incubation (8, 9, 11). Typically, only a small fraction of blood culture bottles in patients with HACEK-linked IE demonstrate growth, and the HACEK group is often associated with culture-negative IE cases (5). Furthermore, capsular material from this organism has been thought to be a potent mediator of bone resorption (14). This implies that *A. actinomycetemcomitans* can cause bone infection in the setting of bacteremia. Thus, there may be latent *A. actinomycetemcomitans* spondylitis cases considering the fastidious character and virulence of the pathogen.

Second, concurrent IE may be present in patients with pyogenic spondylitis caused by *A. actinomycetemcomitans*. In general, vertebral spondylitis is a complication of bacteremia, and associated endocarditis is seen in some patients. A retrospective review including 91 cases of vertebral spondylitis identified 28 patients (31%) with IE (15). Although none of the five previously described cases of pyogenic spondylitis due to *A. actinomycetemcomitans* had an IE complication (8-12), bacteremia caused by a HACEK organism is highly suggestive of IE. In addition, *A. actinomycetemcomitans* is most commonly involved in IE compared to the rest of the HACEK group (16, 17). Although TEE detected no apparent vegetation, IE was "possible" in this patient because the blood culture yielded *A. actinomycetemcomitans*, and the patient had a prosthetic valve, which satisfies one major (blood cultures) and one minor (predisposing heart condition) modified Duke criterion (2). Furthermore, the patient had two of the risk factors for *A. actinomycetemcomitans* endocarditis: a history of valve damage or valve replacement surgery and dental disease (17). An evaluation for concurrent IE is warranted even though the duration of therapy for pyogenic spondylitis is adequate for the treatment of IE in most cases (3-7). Patients with IE require additional follow-up evaluations for valvular disease as well as prophylactic antibiotics for the prevention of subsequent IE.

Finally, the present patient's clinical course suggested that an extended incubation period and repeated sampling for cultures would be required for the detection and identification of *A. actinomycetemcomitans*. In this patient, blood culture from the outpatient clinic was negative after seven days of incubation. The second and third blood cultures were obtained on admission and hospital day 5, respectively. The third culture was positive for Gram-negative rods (GNRs) after four-day incubation, while the second culture remained negative at that point. We requested two-week incubation of

Table 2. Susceptibility Test Results.

Antimicrobial agents	MIC (μg/mL)	Susceptibility
Ampicillin	1	S
Sulbactam/ampicillin	1	S
Cefotaxime	<0.25	S
Ceftriaxone	<0.25	S
Meropenem	<0.125	S
Clarithromycin	8	S
Levofloxacin	<0.5	S
Sulfamethoxazole/trimethoprim	<10	S

The identified organism was susceptible to all of the above listed antimicrobial agents. An "ID test HN20 rapid" panel and mass spectrometry were used to identify the bacterial species. In addition, the MIC obtained by the broth microdilution method and the CLSI (The Clinical & Laboratory Standards Institute) M45 breakpoints were referred to in determining the susceptibility. S: susceptible, MIC: minimum inhibitory concentration

Table 3. Previously Reported Pyogenic *A. actinomycetemcomitans* Spondylitis Cases.

Case	Age/Sex	Endocarditis	Complicaton	Treatment	Reference
1	45/M	Evaluated but no evidence of IE	axillary abscess	ampicillin 6 weeks	8
2	66/M	Not mentioned	nil	cefotaxime 2 weeks → amoxycillin 4 weeks	9
3	65/M	Not mentioned	nil	antibiotic (detail unknown) 6 weeks	10
4	72/M	Evaluated but no evidence of IE	epidural abscess	debridement + ceftriaxone 6 weeks	11
5	52/F	Evaluated but no evidence of IE	nil	ceftriaxone 4 weeks → levofloxacin 6 weeks	12

F: female, M: male, IE: infective endocarditis

the second culture because the patient had a prosthetic heart valve and HACEK infection was possible. Later, the second culture proved positive for GNRs as well, requiring over a week of incubation time. The GNRs were subsequently identified as *A. actinomycetemcomitans*. Recent studies have shown that HACEK bacteria can be isolated using standard culture methods and media within a standard five-day incubation period (18, 19). However, our case required a longer incubation period and repeated cultures before growth was detected. A review of 102 IE cases also found that the mean duration to obtain a positive blood culture was 7.1 days, with a range of 1-15 days. Therefore, extended incubation and repeated blood cultures should be considered if a HACEK infection is suspected.

In conclusion, although the frequency is low, *A. actinomycetemcomitans* can cause pyogenic spondylitis and concurrent IE. There may therefore be latent *A. actinomycetemcomitans*-mediated spondylitis cases. Patients with spondylitis, a history of heart valve disease and extensive dental disease, and for whom blood cultures remain negative might have infection caused by *A. actinomycetemcomitans*. Upon presentation of these signs, extended incubation and repeated blood cultures must be employed to detect and identify the pathogenic organism. Further research is needed to obtain a reliable estimate of the frequency of *A. actinomycetemcomitans* spondylitis and the coexistence of IE.

The authors state that they have no Conflict of Interest (COI).

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