Vertebral osteomyelitis caused by the novel pathogen *Cutibacterium modestum*: a case report

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**Abstract**

**Background:** *Cutibacterium modestum* is one of the five species of the genus *Cutibacterium*. While *C. acnes* has been reported as an important pathogen in bone and joint infections, the clinical characteristics of *C. modestum* infections remain unclear. Moreover, thus far, there has been no clinical case report regarding *C. modestum* infections.

**Case presentation:** An 82-year-old man with a history of repeated trigger point injections for lumbago at the L4 level presented with fever and an exacerbation of lumbago. Physical examination indicated knocking pain at the L4–L5 levels; magnetic resonance imaging showed irregular bone destruction of the L4 vertebral body, and low T1 and high T2 intensity lesions at the L4–L5 intervertebral disc. Two sets of blood cultures (two aerobic and two anaerobic) were performed. Intravenous cefazolin was administered, considering the common pathogens of vertebral osteomyelitis, such as *Staphylococcus aureus*. The patient’s condition did not improve; thereafter, anaerobic culture bottles revealed Gram-positive rods on day 11 of incubation. There was no evidence of infective endocarditis upon transthoracic echocardiography. Needle aspiration from the L4–L5 intervertebral disc was performed on day 13 that also showed the presence of Gram-positive rods. The patient was diagnosed with vertebral osteomyelitis caused by *C. modestum* using a combination of characteristic peak analysis with matrix-assisted laser desorption ionization (MALDI), microbial biochemistry examinations, and 16S rRNA gene sequencing from the blood and pus cultures. He was successfully treated with alternative intravenous ampicillin, followed by oral amoxicillin for 10 weeks, according to the tests for ampicillin susceptibility, with a minimum inhibitory concentration of 0.016 μg/mL using E-test® under aerobic conditions.

**Conclusions:** *Cutibacterium modestum* is a microorganism that is difficult to identify. A combination of characteristic peaks with MALDI, appropriate microbial biochemical examinations, and 16S rRNA gene sequencing may serve as an efficient guide for the identification of *C. modestum*.

**Keywords:** *Cutibacterium modestum*, Vertebral osteomyelitis, MALDI, Microbial biochemistry, 16S rRNA gene sequencing, Heterogeneous, Case report

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**Background**

Bacterial species from the genus *Cutibacterium* are Gram-positive, non-spore forming, non-motile rods, which were reclassified from *Propionibacterium* species, based on whole-genome sequencing results [1, 2]. *Cutibacterium modestum*, which was previously known as *Propionibacterium humerusii*, is one of the five species.
of the genus *Cutibacterium*; it was first reported in 2011 [3]. There is no clinical case report on *C. modestum* infections, and the clinical characteristics of *C. modestum* infections remain unclear. However, *C. acnes*, which belongs to the same subspecies as *C. modestum*, is well recognized as an important pathogen in bone and joint infections, especially in joints with implants [4, 5]. There are methods to identify *C. modestum* microbiologically [6]; however, a comprehensive analysis using various methods is essential for identifying *C. modestum*.

**Case presentation**

An 82-year-old Japanese man, with a history of repeated trigger point injections for lumbago at the L4 level for the past 6 months, presented with fever and exacerbation of his lumbago within the previous month.

Physical examination indicated knocking pain at the L4–L5 levels. The laboratory findings were as follows: C-reactive protein, 20.4 mg/L; and white blood cell count, 7200/µL with 57.1% neutrophils. Magnetic resonance imaging (MRI) showed irregular bone destruction at the L4 vertebral body endplate and a lesion with low T1 and high T2 intensity at the L4 vertebral body and the L4–L5 intervertebral disc (Fig. 1A, B). There was no evidence of infective endocarditis upon transthoracic echocardiography.

Two sets of blood cultures (two aerobic and anaerobic) were performed, and intravenous cefazolin (1 g) was administered every 12 h, considering possible infection with *S. aureus*, a pathogen of vertebral osteomyelitis. He developed pyrexia with persistent lumbago following admission; however, blood culture results remained negative until day 10. Anaerobic culture bottles showed positive results on day 11 of incubation, despite negative results in the aerobic bottles; Gram-positive rods were observed (Fig. 1C). Needle aspiration from the L4–L5 intervertebral disc was performed on day 13, and Gram-positive rods were observed. The isolates were cultured on trypticase soy agar with 5% sheep blood (Nihon Bec-ton–Dickinson, Tokyo, Japan) for 5 days at 37 °C under anaerobic conditions; they formed non-hemolytic and circular white shiny colonies (Fig. 1D). The isolates from blood and pus cultures were identified as *C. modestum* using 16S rRNA gene sequencing, and analysis using the GenBank Basic Local Alignment Search Tool indicated 99.9% (with identities 1433/1435, gaps 0/1435) and 100% (with identities 1417/1417, gaps 0/1417) similarity to *C. modestum*, (GenBank accession no. LC466959),

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**Fig. 1** Radiological and microbiological findings. **A, B** MRI showed irregular bone destruction at the L4 vertebral body endplate (white arrow) with a T2-weighted image (B) and a lesion with low T1 (A) and high T2 intensity (B) at the L4 vertebral body and L4–L5 intervertebral disc (red and yellow arrows). **C–E** Gram staining (×1000) revealed Gram-positive rods (yellow arrow) (C). Non-hemolytic and circular white shiny colonies were observed (D). The susceptibility testing of the isolates from blood culture using the E-test® (bioMérieux) revealed susceptibility to penicillin and ampicillin, with MICs of less than 0.016 and 0.016 µg/mL, respectively, according to the Clinical and Laboratory Standards Institute criteria (M100-S31) (E). F, G The MALDI spectrum of the isolate obtained from blood (F) and pus (G) revealed dominant peaks at 3494, 3713, 6989, and 7429 m/z, respectively. These peaks were not seen for other *Cutibacterium* species, including *C. acnes*. 
respectively [7]. The isolates showed susceptibility to ampicillin, with a minimum inhibitory concentration of 0.016 µg/mL using E-test® (bioMérieux, Marcy l’Etoile, France) under anaerobic conditions (Fig. 1E).

Our patient was diagnosed with vertebral osteomyelitis caused by *C. modestum*, and cefazolin was replaced with intravenous ampicillin (2 g) administration every 6 h, based on the result of the susceptibility test on day 26 (Fig. 2). He became afebrile with relief from lumbago and was discharged with a prescription for oral amoxicillin (1500 mg) every day, on day 45. Amoxicillin was discontinued on day 96, and the patient remained disease-free without recurrence and sequelae.

**Discussion and conclusions**

There are three clinical issues: (1) the possibility of vertebral osteomyelitis caused by *C. modestum* in clinical settings, (2) methods to identify *C. modestum* and the potential of heterogeneity of *C. modestum*, and (3) clinical management of vertebral osteomyelitis caused by *C. modestum*.

*C. modestum* is widely recognized as a postoperatively contracted causative agent of vertebral osteomyelitis [8]. *C. modestum* is an anaerobic, aerotolerant, and non-spore-forming Gram-positive rod [6]. The isolates form non-hemolytic, circular white shiny colonies that are 1.0 × 1.5 mm in size on trypticase soy agar with 5% sheep blood (Nihon Becton–Dickinson) after culture for 5–7 days at 30–37 °C under anaerobic conditions [6]. *C. modestum* is a skin commensal, similar to *C. acnes*; therefore, *C. modestum* could also cause infections via contaminated skin surfaces [1, 6]. Our patient underwent repeated trigger point injections before admission. This is the most plausible source of the infection in this case. *C. modestum* could be misidentified as *C. acnes*, based on the low score value of < 1.70 when using matrix-assisted laser desorption ionization (MALDI) [6]. The database of the MALDI biotyper® (Bruker Daltonik GmbH, Bremen, Germany) lacks the spectrum of *C. modestum* [6]. Additionally, *C. modestum* shows 98.0% similarity to *C. acnes* in 16S rRNA gene sequencing [6]. Therefore, several *C. acnes* infections in previously published case reports could have been *C. modestum* infections.

There are three keys to identify *C. modestum*. First, the dominant peaks in the MALDI spectrum of *C. modestum* are present at 3493, 3712, 6986, and 7424 m/z, which are absent in that of *C. acnes* [6, 9]. This suggests the involvement of *C. modestum* in cases with other *Cutibacterium* species, based on the low scores in MALDI. In our case, the isolates from blood and pus showed a low score value of 1.55 and 1.45, respectively, to *C. acnes* with MALDI biotyper® (Bruker). However, the MALDI spectrum of isolates from blood and pus exhibited dominant peaks...
of 3494, 3713, 6989, and 7427 m/z and 3495, 3714, 6991, and 7429 m/z, respectively (Fig. 1F, G).

Second, C. acnes is divided into three subspecies: C. acnes subspecies acnes, C. acnes subspecies defendens, and C. acnes subspecies elongatum. Unlike C. modestum, C. acnes subspecies acnes and C. acnes subspecies defendens grow well even under aerobic conditions [6]. C. modestum could also grow aerobically; however, the growth is limited, similar to that of C. acnes subspecies elongatum [6]. This could be used to distinguish C. modestum from other Cutibacterium species, which show similarity upon 16S rRNA gene sequencing.

Third, the microbial biochemistry of C. modestum is unique. C. modestum (LC466959) shows negative results for hydrolysis of N-acetyl-β-glucosaminidase, indole, phenylalanine arylamidase, leucine arylamidase, pyrazinamidase, β-glucuronidase, β-galactosidase, and gelatin and for ribose fermentation; the other Cutibacterium species show variable results [6]. This is useful in identifying C. modestum. In our case, the isolates were positive for indole hydrolysis and negative for hydrolysis of other test substrates. This suggests that C. modestum could comprise heterogeneous strains.

These characteristics, in addition to the culture period, characteristic colonies, and the finding of Gram staining, contribute to the rapid identification of C. modestum, even in cases without 16S rRNA gene sequencing.

Clinically, blood cultures are often negative in C. acnes vertebral osteomyelitis [10]. Therefore, blood cultures could yield negative results for C. modestum vertebral osteomyelitis. In our case, the anaerobic culture bottles revealed positive results after 11 days of incubation with no preceding antimicrobial administration. Additionally, the needle-aspirated sample from the infected intervertebral disc, obtained on day 13, yielded a positive culture result. The review of 29 C. acnes vertebral osteomyelitis cases indicated that the incubation time for the blood cultures was unknown in cases of negative blood cultures [10]. Although this is one case and there is no detailed clinical case report of C. modestum vertebral osteomyelitis, these findings suggest the importance of prolonged cultures and local needle aspiration in cases of negative blood cultures for identifying C. modestum.

The optimal duration of antimicrobial therapy for C. modestum vertebral osteomyelitis is uncertain. In vitro, C. acnes could survive on Schaedler medium for 8 months under anaerobic conditions; the conditions are similar in the vertebrae or intervertebral discs [11]. Our patient was successfully treated with the appropriate antibiotics for 10 weeks. Antibiotic therapy for a mean duration of 8.7 weeks (range 2–28 weeks) has resulted in good outcomes in 45/46 (98%) cases, among the 51 reported cases of C. acnes vertebral osteomyelitis [10]. This suggests that the duration of antimicrobial therapy in our case was appropriate, despite the results in vitro.

In conclusion, C. modestum is a difficult-to-identify pathogen mimicking C. acnes with regard to its microbiological characteristics. However, a combination of characteristic peak analysis with MALDI, appropriate microbial biochemistry examinations, and 16S rRNA gene sequencing may serve as a reliable and efficient guide for identifying and diagnosing C. modestum infections.

Abbreviations
MALDI: Matrix-assisted laser desorption ionization; MRI: Magnetic resonance imaging.

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Authors’ contributions
HT1: contributed to the clinical management of the patient and was involved in study conception, acquisition and analysis of the data, and drafting of the manuscript. KT: contributed to the acquisition and analysis of the data and was involved in the supervision of the drafting and critical revision of the manuscript. NM and CI: contributed to the acquisition and analysis of the data. HT2 and YN: involved in the study conception. TM and SS: involved in the supervision of the drafting and critical revision of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets generated and/or analysed during the current study are included in the manuscript.

Declarations
Ethics approval and consent to participate
This study has been approved by the institutional review board and ethics committee of Japanese Red Cross Ise Hospital (Permission Number: ER2020-111).

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Competing interests
The authors state that they have no competing interests.

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