Pyogenic Spondylitis and Diskitis Caused by *Helicobacter cinaedi* in an Immunocompetent Adult Patient

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**Abstract**

We herein describe the first reported case of pyogenic spondylitis and diskitis caused by *Helicobacter cinaedi*. The results of magnetic resonance imaging and the histology of biopsied tissue were suggestive of acute infection at the lumbar spine. The pathogen was obtained by a blood culture examination and identified by 16S rRNA analysis. Eight weeks of antibiotics therapy resulted in a good clinical course. *H. cinaedi* infections have been increasingly reported in recent years, but the pathogen’s epidemiological and pathological characteristics are still unclear. One of the difficulties in understanding the pathogenesis of *H. cinaedi* has been the challenges in cultivating the pathogen. Novel strategies for the diagnosis of *H. cinaedi* must be developed.

**Key words:** BacT/ALERT, bacteremia, *Helicobacter cinaedi*, spondylitis, zoonosis

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**Introduction**

*Helicobacter cinaedi* is a gram-negative spiral or fusiform rod-type bacterium, belonging to the family of *Helicobacteraceae* that resides in the gastrointestinal tract of humans or animals (1, 2). *H. cinaedi* infection was first reported as gastroenteritis in a homosexual man in 1984 (3). In Japan, the first case of *H. cinaedi* infection was described in 2003 in a patient undergoing immunosuppressive therapy after renal transplantation (4). Since then, *H. cinaedi* infections have been increasingly reported (5, 6). However, according to a prospective study on 13 Japanese medical facilities, only 0.036% (6/16, 743) of the blood culture examinations tested positive for *H. cinaedi* (7). Hence, the incidence of *H. cinaedi* bacteremia is very low, and its epidemiological and pathophysiological characteristics are still not well known.

*H. cinaedi* often causes cellulitis and bacteremia (8), and less frequently gastroenteritis (3, 8) and meningitis (9). To the best of our knowledge, no cases of pyogenic spondylitis and diskitis associated with *H. cinaedi* infections have been reported to date. We herein describe the first such case caused by *H. cinaedi*.

**Case Report**

A 64-year-old man without remarkable underlying disease was admitted to our hospital due to acute-onset high fever (body temperature: 38.8°C) and lower back pain that exacerbated with movement. He had not taken any medication but had close contact with a dog at his home. Other than the back pain, the patient had no other specific symptoms including traumatic or skin lesions. A physical examination did not reveal any particular findings. The laboratory data obtained on the day of admission revealed a white blood cell count of 15,100/μL with 87.5% neutrophils, a C-reactive protein level of 18 mg/dL, and a procalcitonin level of 0.14 ng/mL. The computed tomography scan did not show any pathogenic lesions. However, further investigation by magnetic resonance imaging (MRI) was suggestive of acute in-

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Sequence data were analyzed using the Basic Local Alignment Search Tool (BLAST) sequence homology search program at GenBank, and the organism was confirmed to have a 99.76% (1295/1298 bps) sequence homology with the published sequence of the reference H. cinaedi strain (GenBank Accession No. AY631947.1). Due to technical difficulties, the drug susceptibility testing could not determine the minimal inhibitory concentration (MIC) of the antibiotics.

Based on the results of our systemic investigation, a final diagnosis of pyogenic spondylitis and diskitis caused by H. cinaedi was made, although the pathogen was not detected in the biopsied tissues. An attending doctor changed the antibiotic therapy to a combination of cefazolin and intravenous fosfomycin (1 g, twice daily). The patient’s symptoms gradually improved, and he was discharged after 8 weeks. No other patients with H. cinaedi infection were observed in the hospital while this patient was hospitalized.

**Discussion**

We herein described a case of pyogenic spondylitis and diskitis caused by H. cinaedi infection in an adult immunocompetent patient. Although the pathogen was not detected in the surgical specimen, MRI and histology results showed inflammatory changes that were consistent with acute bacterial infection. With the exception of the blood samples, bacteria are routinely cultured for only three days at our laboratory, which could explain the negative result from the biopsied specimen.

H. cinaedi infection is typically thought to occur in immunocompromised patients [e.g., those with chronic kidney disease (11), diabetes mellitus (11), malignant disease (5, 11), renal transplantation (4), and human immunodeficiency virus infection (8)]. Recently, immunocompetent patients have also been shown to be infected with H. cinaedi (6), and nosocomial infections with H. cinaedi have been reported (4, 12). Notably, a H. cinaedi outbreak after orthopedic surgery has been recently described (6).

The source of the H. cinaedi infection in our patient could not be determined. He was not immunocompromised, nor did he have a history of human immunodeficiency virus infection in the lumbar spine (Fig. 1). Echocardiography was not performed. On day 2 after admission, percutaneous discectomy was performed due to suspecting pyogenic diskitis. Although no pathogens were detected in the surgical specimen, a histopathological examination showed an infiltration of neutrophils in the intervertebral disc. The patient was placed on intravenous cefazolin (1 g, four times daily) after the surgery.

Two sets of blood cultures were obtained on the day of admission and one of them became positive for gram-negative spiral rods on day 5 (BacT/Alert 3D system, Sysmex bioMerieux, Tokyo, Japan) (Fig. 2). The organism could not be identified by the MicroScan Walkaway 40 SI system (Siemens Healthcare Diagnostics, Tokyo, Japan) and hence was subjected to a partial 16s rRNA sequence analysis. The QIAamp DNA mini kit (QIAGEN, Hilden, Germany) was used for DNA extraction, and amplification was performed with a GeneAmp PCR 9700 thermocycler (Applied Biosystems, Foster City, USA) using the primers 27f (5'-AGA GTT TGA TCC TGG CTC AG-3') and 1492r (5'-GGT TAC CTT GGT ACG ACT T-3') (10). The polymerase chain reaction (PCR) protocol was composed of 30 cycles of denaturation (94°C for 30 seconds), primer annealing (53°C for 30 seconds) and extension (72°C for 90 seconds), followed by an extension step at 72°C for 7 minutes. Purification of the amplicon was performed with the AMPure PCR purification system (Agencourt, Beverly, USA) according to the manufacturer’s instructions. The PCR products were then sequenced with the ABI Prism BigDye Terminator v3.1 cycle sequencing ready reaction kit (Applied Biosystems) and the 3130xl Genetic Analyzer (Applied Biosystems). The sequence data were analyzed using the Basic Local Alignment Search Tool (BLAST) sequence homology search tool.
infections. Instead, he may have been infected with *H. cinaedi* through animal contact at home. *H. cinaedi* has been isolated from pet and farm animals (2, 13), and previous studies have suggested the possibility of zoonotic transmission through animal contact (14, 15). Alternatively, bacterial translocation from the gastrointestinal tract may have caused the infection of the spinal cord. Araoka et al. reported that 56% of patients with *H. cinaedi* bacteremia were positive for *H. cinaedi* in their stool samples (11).

*H. cinaedi* is known to be hard to cultivate (16). Therefore, many cases of *H. cinaedi* infections may have gone unnoticed. Since the pathogen often causes bacteremia, the blood culture is the most important method used for the diagnosis. Generally, a long incubation period is needed for *H. cinaedi* detection (8, 16), and the detection rate in blood cultures varies depending on the automatic blood culture system used. In the BACTEC system (Becton, Dickinson and Company, Sparks, USA), approximately 50% of cases were reported to require an incubation period of 5 or more days, and 13% required cultivation of more than 1 week (11). In contrast, it has been suggested that the BacT/ALERT system is not adequate for detecting *H. cinaedi* (17). However, in our case, the BacT/ALERT system successfully detected *H. cinaedi* with an incubation period of 5 days. Of note, Tomida et al. reported that the VersaTREK system (TREK Diagnostics, Cleveland, USA) that was recently introduced in Japan could detect *H. cinaedi* within 3 days (18).

At present, there are no available guidelines regarding the susceptibility testing, MIC breakpoints and treatment strategies for *H. cinaedi* infections. In the present case, we successfully treated the patient with a combination of cefazolin and fosfomycin. *H. cinaedi* is typically susceptible to carbapenems, aminoglycosides and tetracycline, while highly resistant to macrolides (17). A moderate MIC has been reported for penicillins and cephalosporins (19). Fluoroquinolones were previously considered to be effective for treatment, however, recently isolated *H. cinaedi* strains have been reported to be resistant to this drug (20). The susceptibility testing for fosfomycin has not been reported. Considering the clinical course of *H. cinaedi* infection, we suggest that fosfomycin may be an alternative treatment agent for *H. cinaedi* infections. The effectiveness of fosfomycin for the treatment of *H. cinaedi* infection should be established.

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

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