Vertebral Osteomyelitis Caused by *Helicobacter cinaedi*

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*Helicobacter cinaedi* causes bacteremia, cellulitis, and gastroenteritis. We report the first case of vertebral osteomyelitis caused by *H. cinaedi* in an elderly man with low back pain and fever. The pathogen was detected in blood and lumbar disc, and the infection was successfully treated with oral doxycycline for 11 weeks.

CASE REPORT

A 66-year-old man presented at our hospital due to a 2-week history of low back pain and fever accompanied by shaking chills. Two days previously, he had erythema on his body trunk and both lower extremities, which disappeared spontaneously. He had a history of diabetes mellitus and liver cirrhosis with esophageal and gastric varix, for which he was being treated with gliimpiridine at another hospital. His HbA1c level was 6.9%, and his Child-Pugh score was class B. He had no remarkable family history. He owned a pet cat that sometimes bit his hands.

On physical examination, his body temperature was 37.2°C, blood pressure was 130/65 mm Hg, pulse rate was 107 beats/min, and respiratory rate was 12 breaths/min. His breath and heart sound were normal, and his abdomen was soft. He had no vertebral and paravertebral muscle tenderness. All neurological findings were normal. He had no rash. Laboratory tests showed an elevated white blood cell (WBC) count of 12.2 × 10³/μl and C-reactive protein (CRP) level of 7.74 mg/dl. Two sets of blood cultures were obtained using Bactec Plus Aerobic/F and Anaerobic/F culture bottles (Becton, Dickinson and Company, Sparks, MD). After 4 days of incubation, Gram-negative spiral bacteria were detected in two sets of aerobic blood bottles. A microaerobic culture was conducted at 35 ± 2°C under 5% CO₂. The strains formed distinctive film-like colonies on chocolate II agar (Nippon Becton, Dickinson and Company, Tokyo, Japan) and Vitalmedia sheep blood agar (Kyokuto Pharmaceutical Industrial Co., Ltd., Japan). Multiplex PCR was performed with colonies from subcultures in accordance with previously published methods (1, 2), using 5'-TATACCGTTAGGAGCTGGA-3' and 5'-ATCAATTAACTCGAGCACC-3' as primers to amplify the 23S rRNA gene region common to all types of *Helicobacter* bacteria. We also used the primers 5'-AGGGATTCCACAAGTGAGC-3' and 5'-TTCTGTCTGTGCGTTCATC-3' to amplify the *gyrB* gene region, which is specific only to *Helicobacter cinaedi* (1). This is also recommended in CLSI MM-18A (3). We identified the bacteria as *H. cinaedi* because they had both genes amplified. Treatment with oral amoxicillin at 500 mg three times a day was initiated. However, 24 days after the initial positive blood culture, repeated blood cultures continued to be positive for *H. cinaedi*. The patient’s low back pain and low-grade fever persisted. His WBC count was 7.5 × 10³/μl, and the CRP level was 1.73 mg/dl. Magnetic resonance imaging (MRI) of the lumbar spine was performed, which revealed spondylodiscitis and discitis of lumbar vertebrae (L1) and L2 (Fig. 1). We stopped prescribing amoxicillin for 1 week and performed an aspiration biopsy of his lumbar disc on day 6 after admission. We extracted DNA from the specimen using a QIAamp DNA minikit (Qiagen K.K., Tokyo, Japan) and amplified it by PCR using the same method as blood cultures. The PCR detected the *gyrB* gene region specific to *H. cinaedi* in the specimen. Bacteria were not observed by Gram stain of the specimen. The aspirated material was directly inoculated on chocolate II agar and Vitalmedia sheep blood agar, followed by microaerobic culture at 35 ± 2°C under 5% CO₂. It became positive for *H. cinaedi* after 13 days of incubation. Therefore, we diagnosed him with vertebral osteomyelitis caused by *H. cinaedi* accompanied by bacteremia. After lumbar disc biopsy, we started treatment with intravenous ampicillin at 2 g every 6 h. However, even after 7 days of treatment, his low back pain and fever persisted, and the CRP level was still 2.03 mg/dl (Fig. 2). On day 14, we changed the antibiotic from ampicillin to oral doxycycline at 100 mg twice a day. After initiation of doxycycline, he became afebrile and his low back pain was alleviated. His CRP returned to normal levels, and blood cultures were negative at this time. He was discharged on day 25. Antibiotic treatment with the same regimen was continued for 11 weeks, and he had no symptom recurrence.

The course of this patient highlights two important clinical issues: *H. cinaedi* can cause vertebral osteomyelitis, and this infection can be successfully treated with oral doxycycline for prolonged periods.

First, *H. cinaedi* can cause vertebral osteomyelitis. The present patient developed bacteremia and vertebral osteomyelitis due to *H. cinaedi*, which was confirmed by low back pain, fever, elevated WBC and CRP, and lumbar MRI findings together with isolation and identification of *H. cinaedi* from blood and lumbar disc. *H. cinaedi* infections typically present as bacteremia (1, 2, 4) with or without cellulitis. It also causes gastroenteritis (4, 5), meningitis...
(6, 7), arthritis (8), and infective endocarditis (9). This is the first case demonstrating that *H. cinaedi* was capable of causing vertebral osteomyelitis. We think this osteomyelitis occurred secondarily to bacteremia, because the patient did not have the local soft tissue infection that might directly infiltrate into bones. We do not know whether this patient had infective endocarditis, because we did not perform echocardiography.

*H. cinaedi* infection occurs primarily in immunocompromised hosts, particularly in men infected with HIV (4, 10). Less commonly, infection can be observed in patients with alcoholism, diabetes, or malignancy and occasionally in immunocompetent patients (1, 11–13). Prior contact with animals has been reported in *H. cinaedi*-infected patients (4, 8), suggesting that contact with carrier animals may be a route of transmission for this pathogen. The patient in this case had three risk factors of *H. cinaedi* infection: diabetes mellitus, liver cirrhosis, and animal contact with his cat.

Second, this case of vertebral osteomyelitis was successfully treated with oral doxycycline for prolonged periods. No guidelines have been developed with respect to choice or duration of antibiotic treatment of *H. cinaedi* infections. An epidemiologic study of patients with *H. cinaedi*-associated illness (4) reported that treatment with penicillin, tetracycline, or aminoglycoside may be more effective than treatment with cephalosporins, erythromycin, or ciprofloxacin. Moreover, various isolates of *H. cinaedi* in Japan have shown increased resistance to penicillins, macrolides, and quinolones (14). In the present case, amoxicillin and ampicillin decreased the CRP level to some extent; however, the patient’s low back pain and fever were not alleviated, and blood culture continued to be positive during the treatment. In contrast, after initiation of treatment with doxycycline, his symptoms improved and blood culture became negative. In this case, amoxicillin and ampicillin seem not to have worked enough; however, doxycycline seems to have been more effective. The concentration of doxycycline in bone has been reported to range from as low as 2% to as high as 86% of serum levels (15). We do not know the concentration in bone in this case. The antimicrobial susceptibility of *H. cinaedi* in this case is shown in Table 1. We could not check the MIC of doxycycline; however, we used doxycycline with reference to previous reports (4, 11). As for the duration of treatment, it has been reported that long-term treatment (2 to 6 weeks) was superior to short-term treatment (≤10 days) (4). Remission is usually obtained with antibiotic administration after approximately 1 to 5 weeks (1). Because our patient not only had *H. cinaedi* infection but also vertebral osteomyelitis, we treated him with antibiotics for a long time. Doxycycline was prescribed at 100 mg twice a day for 11 weeks in total.

In conclusion, we identified *H. cinaedi* as a causative agent of vertebral osteomyelitis, which was successfully treated with oral doxycycline for prolonged periods. Physicians should consider *H. cinaedi* a possible pathogen for vertebral osteomyelitis.

### TABLE 1 Antimicrobial susceptibility of the *H. cinaedi* isolate from the blood culture

<table>
<thead>
<tr>
<th>Antibiotic(s)</th>
<th>MIC (µg/ml)</th>
</tr>
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<tbody>
<tr>
<td>Ampicillin</td>
<td>8</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>8</td>
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<tr>
<td>Meropenem</td>
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<tr>
<td>Erythromycin</td>
<td>&gt;256</td>
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<td>Minocycline</td>
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<tr>
<td>Ciprofloxacin</td>
<td>&gt;32</td>
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<tr>
<td>Trimethoprim-sulfamethoxazole</td>
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REFERENCES


