Recurrent *Helicobacter cinaedi* Cellulitis and Bacteremia in a Patient with Systemic Lupus Erythematosus

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**Abstract**

A 31-year-old woman who had developed systemic lupus erythematosus at 17 years of age was admitted to the hospital for suspected cellulitis in the lower extremities. A blood culture performed upon admission to the hospital detected *Helicobacter cinaedi* (*H. cinaedi*), which was also isolated in blood and fecal cultures obtained on the 42nd hospital day. Bacterial translocation of *H. cinaedi* present in the intestines may have led to the development of recurrent bacteremia and cellulitis. In cases such as this, appropriate antibiotics therapy might be needed for more than one month. Moreover, *H. cinaedi*, a cause of emerging infections, requires a long period of time to grow; therefore it is important to extend the culture duration when the presence of this bacterium is suspected.

**Key words:** aztreonam, bacteremia, cellulitis, emerging infectious disease, *Helicobacter cinaedi*, systemic lupus erythematosus


**Introduction**

*Helicobacter cinaedi* (*H. cinaedi*) infection is an emerging infectious disease that affects immunocompromised patients (1). *H. cinaedi* infections often occur as opportunistic infections resulting from human immunodeficiency virus (HIV)-infection, chronic alcoholism or malignancy with or without the administration of chemotherapy (1, 2). Opportunistic infections are serious complications associated with the treatment of autoimmune diseases with corticosteroids and/or various immunosuppressive agents. This report describes a case of recurrent cellulitis and bacteremia caused by *H. cinaedi* in a patient with systemic lupus erythematosus (SLE).

**Case Report**

The patient was a 31-year-old woman who developed SLE and rheumatoid arthritis (RA) at 17 and 19 years of age, respectively. She had undergone necrotomy at the age of 26 due to necrotizing fasciitis of the right lower extremity caused by a Group A streptococcus infection. She had been taking 12.5 mg/day of prednisolone and 15 mg/week of methotrexate and her SLE and RA were stable. She was admitted to the hospital for suspected cellulitis after developing erythema in the left lower extremity several days prior to admission. Her body temperature was 37.8°C and there was warmth and swelling in both lower extremities that showed erythema with tenderness (Fig. 1). No clear signs of trauma were observed. The patient exhibited a clear consciousness and no obvious chest or abdominal abnormalities were observed. The laboratory data obtained on admission showed: hemoglobin: 12.9 g/dL, platelets: 20.7×10⁴/μL, white blood cell count: 13,500/μL (seg 86%, stab 6%, lym 5%, mono 3%), erythrocyte sedimentation: 43 mm/h, C-reactive protein (CRP): 6.72 mg/dL, IgG: 1,140 mg/dL, IgA: 442 mg/dL, IgM: 109 mg/dL, CH50: 52 U/mL, C3: 135 mg/dL, C4: 33 mg/dL and circulating immune complex: <1.5 μgEq/mL on a C1q binding assay (reference interval: <3.0 μgEq/mL). Tests for rheumatoid factor and anti-nuclear antibodies were positive at 114.0 U/mL and 160× (homogene-
Figure 1. Both lower extremities were warm, swollen, and showed erythema with tenderness. No clear trauma was observed.

Figure 2. Gram stain of blood culture: poor staining of slender spirillum (1,000x).

Table. Antimicrobial Susceptibility of Pathogens Grown on Blood Culture

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>MIC (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ampicillin</td>
<td>1</td>
</tr>
<tr>
<td>cefaclor</td>
<td>16</td>
</tr>
<tr>
<td>cefotiam</td>
<td>16</td>
</tr>
<tr>
<td>imipenem</td>
<td>0.016</td>
</tr>
<tr>
<td>erythromycin</td>
<td>&gt;256</td>
</tr>
<tr>
<td>clarithromycin</td>
<td>&gt;256</td>
</tr>
<tr>
<td>levofloxacin</td>
<td>&gt;32</td>
</tr>
</tbody>
</table>

MIC: minimal inhibitory concentration

Discussion

*H. cinaedi* was originally reported to be a *Campylobacter*-like organism isolated from the blood of homosexual men infected with HIV in 1984 (3). However, *H. cinaedi* was removed from the genus *Campylobacter* and reclassified in 1991 (4). *H. cinaedi* has also been isolated from other immunocompromised patients, including those with chronic alcoholism or malignancy who are or are not receiving chemotherapy. Research has focused on emerging infectious diseases associated with cellulitis, arthritis and bacteremia in immunosuppressed patients (1, 2).

The first case of bacteremia with *H. cinaedi* in Japan occurred in a patient receiving immunosuppressive therapy after undergoing renal transplantation (5). Matsumoto et al. evaluated the prevalence of *H. cinaedi* as a pathogen causing bacteremia by evaluating blood culture samples and reported that bacteremia with *H. cinaedi* is rare but can occur in compromised hosts other than those with HIV infection (6). However, there are no reports of cellulitis or bacteremia occurring in association with *H. cinaedi* in patients with autoimmune diseases who are or are not receiving immunosuppressive therapy. An immune disorder caused by autoimmune diseases (SLE and RA) and the inhibition of cellular immunity induced by immunosuppressive therapy (the peripheral lymphocyte count was decreased to 675/µL on admission) may have been involved in the development of the disease in the present patient.

The route of transmission of *H. cinaedi* and the developmental mechanisms underlying *H. cinaedi* infection are unclear; however, in monkeys and hamsters, *H. cinaedi* is thought to infect via the oral route because of its presence in the intestines (7, 8). Rectal colonization of *H. cinaedi* continues after improvement is seen in the clinical manifestations of infection in experimentally-infected monkeys (9). The route of initial infection in the current case was unclear because the patient had no previous contact with animals and no hospital infections were observed. However, the possibility of nosocomial transmission of *H. cinaedi* has been...
suggested in some reports. Sufficient control of contact infection is necessary (10, 11).

It is highly likely that \textit{H. cinaedi} infections have been overlooked due to the difficulties encountered in culturing the bacterium. Although it is difficult to diagnose \textit{H. cinaedi} infection using standard culture methods, many recent reports have emphasized the importance of diagnosing the disease, especially in immunocompromised patients (5, 12, 13). It is important to avoid overlooking Gram-negative spiral-shaped rods on Gram staining. The culture duration is extended when the presence of \textit{H. cinaedi} is suspected (7-day culture minimum, and approximately 10 days if possible) (2). Careful observation is necessary because \textit{H. cinaedi} grows in a thinly spread layer, a pattern which is markedly different from the colony properties of \textit{H. pylori} (14).

Identification and diagnosis of \textit{H. cinaedi} using electron microscopy, polymerase chain reaction (PCR) analyses and 23S rRNA sequencing techniques have been reported (11, 13, 15, 16). Identification of \textit{H. cinaedi} in the current case was made based on microscopic examinations (Fig. 2), biochemical properties (urease activity was negative) and a PCR (using the forward primer AGGGATTCCA CAAAGTGAGC and the reverse primer TCTTGTCCTGTG CATTCACTC) to amplify the gyrB gene region, which is specific to \textit{H. cinaedi} analysis in accordance with the method presented by Ohkusu et al. (17).

\textit{H. cinaedi} was also isolated in a fecal culture obtained after recurrent bacteremia in this case (Fig. 3). Bacterial translocation of \textit{H. cinaedi} present in the intestines may have led to the development of bacteremia and cellulitis. Moreover, pathogenic \textit{H. cinaedi} produces cytolethal dis tensing toxin, invades tissues via the intestinal mucosa and can cause bacteremia particularly in immunocompromised patients (18, 19).

Uçkay et al. (20) and Sullivan et al. (21) also have reported cases of recurrent \textit{H. cinaedi} cellulitis and bacteremia and both suggested that physicians should focus on determining the adequate dose and duration of antibiotic therapy. Another study reported that long-term treatment (2-6 weeks) was superior to short-term treatment (1). The response to treatment depends on the patient’s systemic condition and immune function; however, remission is usually obtained with antibiotic administration after approximately one to five weeks (11). Treatment should be continued for prolonged periods after blood cultures become negative and cellulitis improves in immunocompromised patients due to the possibility for the presence of residual \textit{H. cinaedi} in the intestines, as in this case (the disease recurred after a 3-week drip infusion of AZC, for which AZC was administered by drip infusion for two weeks followed by oral administration of MINO for four weeks). This report presented a case of recurrent cellulitis and bacteremia caused by \textit{H. cinaedi} in a 31-year-old systemic lupus erythematosus patient.

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

Acknowledgement
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References


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http://www.naika.or.jp/imonline/index.html