

## Short Communication

# The First Case Report of Cerebral Cyst Infection Due to *Helicobacter cinaedi*

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**SUMMARY:** We report the first case of cerebral cyst infection by *Helicobacter cinaedi*, a fastidious spiral-shaped gram-negative rod bacterium. A 70-year-old man visited Tokyo Medical University Hospital with persisting fever since 2 weeks. He underwent surgery and radiotherapy for parapharyngeal space squamous cell carcinoma 10 years ago. The radiotherapy resulted in a cerebral cyst as a side effect, and an Ommaya reservoir was inserted into the cyst. Blood culture and analysis of the brain cyst fluid revealed the presence of spiral-shaped gram-negative rod bacteria, which were identified as *H. cinaedi* by polymerase chain reaction. Initially, we administered clarithromycin (400 mg per day). After *H. cinaedi* infection was confirmed, the treatment was changed to meropenem (MEPM 6 g per day). The patient was treated for 43 days in the hospital with intravenous meropenem, and his clinical course was satisfactory. On the 44th day, he was discharged and prescribed oral minocycline (MINO 200 mg per day). After discharge, the patient's *H. cinaedi* infection did not recur. Our case illustrated the wide clinical spectrum of *H. cinaedi* as well as the effectiveness of antibiotic therapy comprising MERM and MINO for treating central nervous system infection by this organism.

*Helicobacter cinaedi* is a gram-negative spiral-shaped rod bacterium that was first reported in 1984 as a *Campylobacter*-like organism causing gastrointestinal symptoms in homosexual men. Early after its discovery, *H. cinaedi* infections were reported mainly in patients infected with human immunodeficiency virus (HIV). Subsequently, *H. cinaedi* infections have also been detected in non-HIV-infected patients with underlying diseases such as hematological disease, cancer, chronic liver disease, or asplenia, as well as in patients being treated with immunosuppressive drugs. *H. cinaedi* is known as a causative pathogen of bacteremia, cellulitis, gastroenteritis, arthritis, meningitis, and kidney cyst infection. Recently, the number of reports of *H. cinaedi* infection has grown owing to increased recognition of its existence. This has also led to an increase in the range of patients infected, ranging from immunocompromised patients to healthy persons and from the elderly to neonates. In this study, we described the first case of cerebral cyst infection due to *H. cinaedi* in a patient with advanced lung cancer.

A 70-year-old man visited Tokyo Medical University Hospital with fever and stagger persisting for 2 weeks. His temperature had been fluctuating between 37.0 and 38.0°C, and he had vomited several times in the past 2 weeks. He had experienced numbness in both upper limbs because of orthopedic spine disease for the past 7

years, but the numbness had worsened in the past month. He underwent surgery and heavy-ion radiotherapy for parapharyngeal space squamous cell carcinoma 10 years ago. An Ommaya reservoir (subcutaneous intraventricular catheter system) was inserted in a brain cyst that developed as a side effect of the radiotherapy. He was retired, and he lived with his wife, daughter, and dog.

Five days before visiting the hospital, the patient was prescribed sitafloxacin by his local physician. Blood culture sampling was performed during his first visit to the hospital, and sitafloxacin was discontinued the next day. Blood cultures (Becton Dickinson, Franklin Lakes, NJ, USA) resulted in the growth of spiral-shaped gram-negative rod bacteria in aerobic bottles after 6 days. Therefore, the patient was administered clarithromycin (400 mg per day) for one week, but he gradually became less communicative and was unable to maintain his posture. Hence, he was admitted to the hospital for further examination.

On admission, the patient was somnolent and roused by sound. His physical condition was as follows: body temperature, 37.4°C; pulse rate, 83/min; respiratory rate, 16/min; and blood pressure, 139/78 mmHg. Laboratory tests revealed a normal white blood cell count (7,400/ $\mu$ L) and a slightly elevated C-reactive protein level (2.72 mg/dL). Cranial computed tomography (CT) revealed enlargement of the brain cyst and cerebral herniation. Immediately after admission, we performed emergency brain cyst drainage and administered intravenous meropenem (MEPM, 6 g per day). The patient received a 7-week course of MEPM in total. After the drainage, his level of consciousness improved. On the 5th day of hospitalization, the brain cyst infection was confirmed to be caused by *H. cinaedi*. We sought to confirm other infectious foci via CT and scintigraphy, but no other sites of infection

Received January 18, 2016. Accepted June 5, 2016.  
J-STAGE Advance Publication June 30, 2016.  
DOI: 10.7883/yoken.JJID.2016.031

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were found, although a neoplastic lesion was found in the upper left lung. A blood culture obtained on the 7th day was found to be negative for *H. cinaedi*. Antibiotic treatment was then changed from intravenous MEPM to oral minocycline (MINO: 200 mg per day) on the 43rd day. A culture obtained from the brain cyst on the 19th day was also found to be negative for *H. cinaedi*. The patient was discharged on the 44th day with daily oral MINO.

The blood culture obtained on the day of admission revealed spiral-shaped gram-negative rod bacteria. After 6 days of microaerobic incubation at 37°C, film-like colonies grew on 5% sheep blood agar. Polymerase chain reaction (PCR) was performed on specimens obtained from the blood culture and brain cyst fluid, as described previously using primer sequences to amplify the *gyrB* gene region (forward: 5'-AGGGATTCCACAAAGTGAGC-3'; reverse: 5'-TCTTGTCCTGTGCGTTCATC-3'), which definitively identified the presence of *H. cinaedi* (1). Antimicrobial susceptibility testing was performed using the disk method according to the standards of Clinical and Laboratory Standards Institute for *Campylobacter jejuni* and *C. coli* (2). The result of antibiotic susceptibility test of the *H. cinaedi* strain confirmed its susceptibility to MINO and resistance to erythromycin, levofloxacin, and fosfomicin.

The number of reports of *H. cinaedi* infection has recently increased, but its biological characteristics are not fully clarified. Many cases of *H. cinaedi* infection are believed to be overlooked because of the difficulty in diagnosis and because the infection can be treated with general antibiotics. *H. cinaedi* infection may lead to many symptoms, including fever, localized pain, arthralgia, diarrhea, rash, and cholangitis, but these symptoms are not typical. In most cases, including ours, the key to identifying *H. cinaedi* infection is blood culture or the demonstration of bacteremia. However, it is difficult to identify *H. cinaedi* infections without having considered the possibility of this infection, owing to the unique conditions required to culture this bacterium successfully, as well as the requirement of PCR for a definitive diagnosis. Standardized treatment for this infection has not been established. To our knowledge, we encountered the first case of a cerebral cyst infection in the central nervous system due to *H. cinaedi*, which was successfully treated.

Although *H. cinaedi* infection was originally considered an opportunistic infection, some recent reports indicated the existence of *H. cinaedi* carriage in healthy persons (3–5). In addition, in these reports, the authors suggested the possibility of a close association between *H. cinaedi* and human diseases, such as atrial arrhythmia and arteriosclerosis, as well as human-to-human transmission of this bacterium. In our case, we did not consider that our patient might be immunocompromised while he was hospitalized, but after his discharge, we found that he had lung cancer and that he might have been immunocompromised. *H. cinaedi* was isolated from the patient's blood culture and brain cyst fluid. The Ommaya reservoir, which was placed in the patient's brain cyst, is also known to be a risk of infection. To the best of our knowledge, this is the first case report of cerebral cyst infection due to *H. cinaedi*. The source of infection remains unknown. Some reports

noted that many types of animals, such as cats, dogs, hamsters, and monkeys, have *H. cinaedi* colonization in their gastrointestinal tracts. However, we did not investigate whether the patient's dog was infected with *H. cinaedi*. Whether the patient was infected with *H. cinaedi* before he developed a fever remains unclear.

*H. cinaedi* is fastidious, and hence, its isolation requires special care. *H. cinaedi* requires a long period to grow in blood culture exceeding the 5-day duration of monitoring (6) that is used in most facilities. It is difficult to distinguish this bacterium from other enterohepatic *Helicobacter* spp.; therefore, PCR is required to make a definitive diagnosis. Neither a standard method to measure the antimicrobial susceptibility of *H. cinaedi* nor guidelines for the treatment of *H. cinaedi* infections have been established.

Empirically, carbapenems, aminoglycosides, tetracycline, penicillins, and cephalosporin are known to be comparatively effective against *H. cinaedi*. Matsumoto et al. recommended the use of beta-lactams for treating bacteremia due to *H. cinaedi* from their study cases (7). Initially, we thought our patient was infected with microbes of the *Campylobacter* or *Helicobacter* genus, and we chose clarithromycin empirically as a first-line antibiotic. Later, the microbe was found to be *H. cinaedi*, and the treatment was changed to MEPM. The duration of antibiotic treatment required for *H. cinaedi* bacteremia was relatively long in previous reports, reaching 14 weeks in some cases (8). An insufficient duration of antibiotic therapy may result in recurrence of *H. cinaedi* infection (8). We were unsure of the effectiveness of the antibiotic treatment as well as the adequate duration of antibiotic administration for treating central nervous system infection caused by this organism. With continued oral MINO administration, our patient's *H. cinaedi* infection did not recur. After 2 months of rehabilitation, he became ambulatory and was able to communicate smoothly. However, he passed away owing to lung cancer 4 months after being discharged.

We have reported the first case of a brain cyst infection caused by *H. cinaedi*. Our study revealed the wide clinical spectrum of *H. cinaedi* as well as the effectiveness of antibiotic therapy using MEPM and MINO for central nervous system infection caused by this organism. According to a number of recent reports, *H. cinaedi* infections could cause various symptoms and pathological conditions in humans (5,9–15). These findings suggest that *H. cinaedi* has latent pathogenicity beyond our current recognition. We consider that elucidation of the biological characteristics of *H. cinaedi*, as well as its wide host range and pathogenicity, would be helpful for treating the diseases and conditions caused by this bacterium. Further studies on *H. cinaedi* are anticipated in the future.

**Conflict of interest** None to declare.

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