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Research Paper

# A Case Of Recurrent *Helicobacter cinaedi* Prosthetic Joint Infection In An HIV-Infected Man

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## Abstract

We describe the case of an HIV-infected man who developed twice a *Helicobacter cinaedi* prosthetic joint infection. In our knowledge, it is the first case to date. Furthermore, it illustrates the fact that this bacterium is difficult to isolate and that recurrences can occur even after apparently successful treatment.

Key words: *Helicobacter cinaedi*, prosthetic joint infection, recurrence

## Background

*Helicobacter cinaedi* is a Gram-negative spiral bacillus, first identified in 1984 in the gut of HIV-infected patients. The first *H. cinaedi* infections reported in the literature were proctitis, proctocolitis or enterocolitis in homosexual men, that inspired its name, "cinaedus" being the latin word for homosexual. (1). Since then, various clinical presentations, e.g. sepsis, recurrent bacteremia (2), cellulitis (3), endocarditis, central nervous system infections (4), or osteoarticular infections (5,6), have been reported. Implant-associated infections have not yet been described.

Here in, we report a case of recurrent *Helicobacter cinaedi* prosthetic joint infection (PJI).

## Case presentation

A 32-year-old homosexual man, infected with human immunodeficiency virus (HIV) in 2005, was admitted in May 2015 for suspected acute prosthetic left knee infection. He had a history of left femoral osteosarcoma in 1996, treated with chemotherapy and resection surgery. Moderate chronic renal insufficiency developed after chemotherapy (creatinine clearance 60 ml/min). A knee megaprosthesis, implanted in 1997, was exchanged in 2006 because of loosening.

In May 2015, he developed acute left knee inflammatory pain, swelling, functional impairment and high fever (40°C), and was hospitalized. No source of infection was found on clinical examination. Blood tests revealed no hyperleukocytosis but elevated C-reactive protein (CRP; 169 mg/liter). Knee aspiration revealed a turbid joint fluid containing 5500 leukocytes/mm$^3$, with a differential of 75% neutrophils. Joint fluid and blood cultures remained sterile. X-ray of the knee showed no signs of osteitis but radiolucency

under the internal tibial plateau was seen. CD4-lymphocyte count was 370/mm$^3$ and HIV load was 4.4 $\log_{10}$/ml. Empirical intravenous (IV) vancomycin, ceftriaxone and rifampicin were prescribed. Surgery with debridement and implant retention (DAIR) without exchange of mobile parts was performed 2 days after admission. A broad-range polymerase chain reaction (16S rRNA) on joint fluid was performed with the universal primers E8F (5-AGAGTTTGATCMTGGCTAG-3) and 357R (5-TGCTGCCTCCCGTAGGAGT-3) using a sample-specific multiplex identifier for pyrosequencing that confirmed infection with *Helicobacter cinaedi* (7). After one week of IV therapy (vancomycin, ceftriaxone, rifampin), treatment was switched for oral doxycycline and clindamycin for 3 months with a favorable outcome. Antiretroviral therapy with abacavir, lamivudine, dolutegravir was begun in May 2015. In April 2017, his CD4 count was 1200/mm$^3$ and HIV load undetectable. The patient remained asymptomatic for 2 years, CRP was normal.

Two years later, on 1$^{st}$ of May 2017, he again suddenly developed similar symptoms (pain, swelling, functional impairment, high fever) in his left knee. CRP was 200 mg/liter. He was admitted in our unit where knee aspiration showed 13,500 leukocytes/mm$^3$, with a differential of 93% neutrophils. Prolonged culture in enriched medium remained sterile, as did blood cultures. X-rays of the left lower limb showed evident osteolysis under the internal and external tibial plateau but no sign of chronic osteitis (no periosteal bone construction or endosteal osteolysis). The patient underwent a second DAIR without exchange of mobile parts, because of the acute onset, sterile joint-fluid cultures and the difficult-to-change arthroplasty. He received continuous intravenous meropenem (6 g/24 hours for a 55-kg patient) for 2 weeks, followed by an oral regimen with minocycline (300 mg/day) for 10 more weeks. Finally, PCR on joint fluid was positive for *Helicobacter* DNA and sequencing of the *gyrA* gene (F2-QRDR-Hspe TGGGTGATGTRATYGGTAAAT R1-QRDR-Hspe TGATTAAGCCCTCYAARATATG 939 bp) (8) confirmed the presence of *H. cinaedi*. The patient had owned a cat for many years. Cultures of the patient's and the cat's feces, did not grow *H. cinaedi*. In July 2018, more than one year after the second episode, the patient is doing well, he walks more than one kilometer without a stick.

## Discussion and conclusions

We report a case of recurrent *Helicobacter cinaedi* prosthetic joint infection, certainly acquired hematogenously, that occurred in an HIV-infected homosexual man. Fewer than 10 osteoarticular infections caused by this *Helicobacter* species have been published (Table 1) (5-6,9-12). Postoperative infections after orthopedic surgery in immunocompetent patients associated with cellulitis have also been described, but non developed septic arthritis and *H. cinaedi* was exclusively isolated from blood cultures (Table 2) (13-14). Further studies confirmed that *H. cinaedi* infections can be hospital-acquired. Documented asymptomatic carriers among health-care workers could be the source of nosocomial infections (1,14-15).

**Table 1:** Case reports of *Helicobacter cinaedi* bone and joint infections

| Study (reference) | Patient | Infection site and clinical signs | Treatment Outcome |
|---|---|---|---|
| Burman et al. Clin Infect Dis. 1995 (10) | HIV-infected men | Two cases of reactive monoarticular arthritis of large joints Cellulitis, mild fever | Not mentioned |
| Vandamme et al. J Clin Microbiol. 1990 (11) | HIV-infected men | Septic monoarticular arthritis of the knee and hip (one case each), Mild fever | Not mentioned |
| Lasry et al. Clin Infect Dis. 2000 (6) | A 20 year old immunocompetent heterosexual man | Monoarticular arthritis of the knee, Mild fever | Rifampicin, ciprofloxacin; 12 weeks. Favorable outcome. |
| Murata et al. Intern Med 2015 (5) | A 56 year old immunocompetent heterosexual man | Vertebral osteomyelitis (C6-C7) Hypothermia | Ceftriaxone; 6 weeks Favorable outcome. |
| Yoshizaki et al. J Clin Microbiol 2015 (9) | A 66 year old man with diabetes mellitus and cirrhosis | Vertebral osteomyelitis (L1-L2), Mild fever | Doxycycline; 6 weeks. Favorable outcome. |
| Hase et al. Intern Med 2018 (12) | A 65 year old immunocompetent heterosexual man | Vertebral osteomyelitis (T11-L2) | Ceftriaxone followed by minocycline; 6 months. Favorable outcome. |

**Table 2:** Cases of postoperative *Helicobacter cinaedi* infections after orthopedic surgery in immunocompetent patients.

| Study (reference) | Type of clean surgery | Clinical presentation | Treatment Outcome |
|---|---|---|---|
| Nielsen et al. BMJ Case Rep 2015 (8) | Arthroscopy of the knee | Arthritis and cellulitis, 30 days after arthroscopy | Rifampin, moxifloxacin; 6 weeks. Favorable outcome |
| Kitamura et al. J Clin Microbiol 2007 (9) | -osteosynthesis of the upper and lower limb (n=6)<br>-knee prosthesis (n=4)<br>-lumbar herniation (n=1) | Eleven cases of cellulitis without arthritis, 8 to 113 days after surgery | Not details<br>4 out of 11 had recurrences of cellulitis |

Our patient developed two similar acute episodes of *H. cinaedi* prosthetic knee infection, separated by a 2-year symptom-free interval. The first episode was certainly an acute hematogenous infection. The second one could be either a relapse due to unsuccessful treatment of the initial infection or a new acute hematogenous infection spreading from a common source. The acute clinical onset after a frank symptom-free interval and the favorable outcome despite retention of the prosthesis, favors the second hypothesis, strengthened by the fact that recurrent infections with this microorganism have been described frequently (2). Comparison of the sequences of both strains couldn't be performed to confirm reinfection with the same or a different strain, because molecular identification was done in 2 different laboratories with different methods. The source of infection could have been the patient's or his cat's gastrointestinal tract but was not confirmed by culture of their feces. Contact with pets such as dogs, cats, rats or hamsters has been described as a risk factor for *H. cinaedi* infection (5).

*H. cinaedi* infection was confirmed in our patient's joint fluid by 16 S rRNA sequencing. Joint aspirate and blood cultures remained sterile, despite prolonged culture duration in enriched medium. *H. cinaedi* isolation is difficult and requires prolonged incubation (4–10 days) and special culture conditions (microaerobic conditions, high humidity) (1). Most of the previous reported cases isolated the microorganism from blood cultures (system BactAlert, BACTEC Plus system, BD BACTEC FX system) (12).

Two surgical strategies were considered to treat our patient's second episode: debridement and DAIR or prosthesis removal with a one-stage exchange. We opted for DAIR, because of the acute clinical onset, no microorganism had been identified during the first week after admission, complete removal and exchange of the megaprosthesis seemed to be difficult; the patient recovered good joint function after a few days of antibiotics.

The optimal antibiotic regimen and its duration for *H. cinaedi* infections have not been clearly defined. *H. cinaedi* has moderate minimal inhibitory concentrations (MICs) for penicillins and cephalosporins, and high MICs for macrolides (1). Fluoroquinolone-resistance is frequent and recurrence after fluoroquinolone therapy has been reported (16). First-choice antibiotics are carbapenems, aminoglycosides and tetracycline. (1). For some authors, meropenem is considered the first-line drug, especially for the treatment of severe infections (4). We treated our patient with initial high-dose intravenous meropenem followed by oral minocycline, for a total of 12 weeks. Treatment duration for previously reported *H. cinaedi* bone-and-joint infections ranged between 6 and 12 weeks.

Our patient's functional and infection-related outcome was very favorable, but follow-up duration is too short to confirm a cure. Recurrences, especially in immunocompromised patients with bacteremia, have been observed in 20% to 60% of them (1, 2, 14, 17). Long-term antibiotic therapy (2–6 weeks) is therefore recommended (1, 18). No recurrence has been observed in patients with bone-and-joint infections but follow-up duration was usually not specified.

In conclusion, *H. cinaedi* is a rare agent of bone-and-joint infections, occurring mostly in immunocompromised patients. This case confirms that it can spread from a distant source and cause recurrent prosthetic joint infection.

## Abbreviations

HIV: human immunodeficiency virus; CRP: C-reactive protein; DAIR: debridement and implant retention; PCR: polymerase chain reaction.

## Authors' contributions

JK, VZ, VM, and SL are the attending physicians for the patient and collected medical data of the patient. BH performed microbiological analysis of the clinical sample. PL and LBB performed the molecular identification of the

second strain. JK and VZ wrote the manuscript. BH, PL, VM, SM and JMZ made a critical revision of this manuscript. All authors read and approved the final manuscript.

## Consent for publication

Written informed consent was obtained from the patient for publication of his medical and personal details.

## Competing Interests

The authors have declared that no competing interest exists.

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