

Getting to the Heart of the Matter: A 20-Year-Old Man With Fever, Rash, and Chest Pain

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Infection with *Helicobacter cinaedi* can encompass a wide spectrum of clinical manifestations, including fever, rash, endocarditis, osteomyelitis, and meningitis. The present case demonstrates the ability of *H cinaedi* to masquerade as acute rheumatic fever and represents the first reported case of cardiac tamponade caused by *H cinaedi*.

Keywords. helicobacter; pericarditis; tamponade; bacteremia.

CASE

A 20-year-old student with no past medical history was seen in the emergency department (ED) for a painful, nodular rash on his left thigh (Figure 1A). He denied fever, sore throat, or recent travel. Antistreptolysin O was 220 IU/mL (normal <100), and he was given intramuscular penicillin G due to concern for acute rheumatic fever. Three weeks later, he returned to the ED with intermittent pleuritic, midsternal chest pain and electrocardiogram findings consistent with acute pericarditis. Despite therapy with ibuprofen and colchicine, his chest pain progressed, and he returned to the ED 1 week later. Exam was notable for a temperature of 38.4°C, tachycardia, distended neck veins, and 2 erythematous nodules on his left thigh. Echocardiogram demonstrated a large pericardial effusion with evidence of tamponade (Figure 1B and Video 1). Peripheral blood cultures were obtained, and he underwent urgent pericardiocentesis of 600 mL bloody fluid.

He was initially treated with penicillin G for presumed acute rheumatic fever. Two days after collection, his blood and

pericardial cultures grew a curved Gram-negative rod that was difficult to visualize on Gram stain but easily seen with carbol fuchsin counterstain (Figure 2A) and acridine orange stain (Figure 2B). The organism grew poorly on *Campylobacter* or *Brucella* blood agar but grew well on buffered charcoal yeast extract agar under microaerophilic conditions. Piperacillin-tazobactam was empirically started.

The patient's fevers resolved by the second day of piperacillin-tazobactam therapy, and repeat blood cultures on day 5 of therapy were negative. Repeat echocardiogram showed complete resolution of the effusion, and the pericardial drain was removed on hospital day 5. Mass spectrometry failed to identify the organism. However, 458 nucleotides of the 16S ribosomal ribonucleic acid (rRNA) sequence matched perfectly with GenBank accession KJ534298 belonging to *Helicobacter cinaedi* strain CIP105369. The working diagnosis was thus changed from acute rheumatic fever to *H cinaedi* bacteremia complicated by purulent bacterial pericarditis. After the organism was identified, the patient was questioned again about his sexual practices. He reported receptive anal intercourse with a man several weeks before admission. Human immunodeficiency virus (HIV) testing by polymerase chain reaction and antibody/antigen screening was negative.

Given his clinical improvement and clearance of cultures, he was discharged on piperacillin-tazobactam to complete a total 4-week course. Based on susceptibility testing by E-test, which was delayed due to slow growth of the organism on susceptibility testing media, he was transitioned to doxycycline monotherapy for the final 2 weeks of treatment (Table 1). Three weeks after completing therapy, he remained asymptomatic, and repeat blood cultures were negative. He was also seen in follow-up 16 months after completing therapy and was doing well without any evidence of relapse.

DISCUSSION

The differential diagnosis for a curved Gram-negative rod that can be cultivated microaerobically is fairly limited and includes species of *Helicobacter*, *Vibrio*, and *Campylobacter*. *Helicobacter cinaedi* is a curved Gram-negative rod first isolated from rectal cultures of men who have sex with men (MSM) [1]. It is considered an "enterohepatic *Helicobacter*" due to its initial isolation from the gastrointestinal tract [2]. The most common presenting symptoms of *H cinaedi* infection are fever and a cellulitic or nodular rash [3, 4], although cases of myopericarditis [5], endocarditis [6], osteomyelitis [7], and meningitis [8] have been reported. Severe disseminated disease has been described in patients with or without immunocompromise. One recent study suggested that patients with community-acquired infections are

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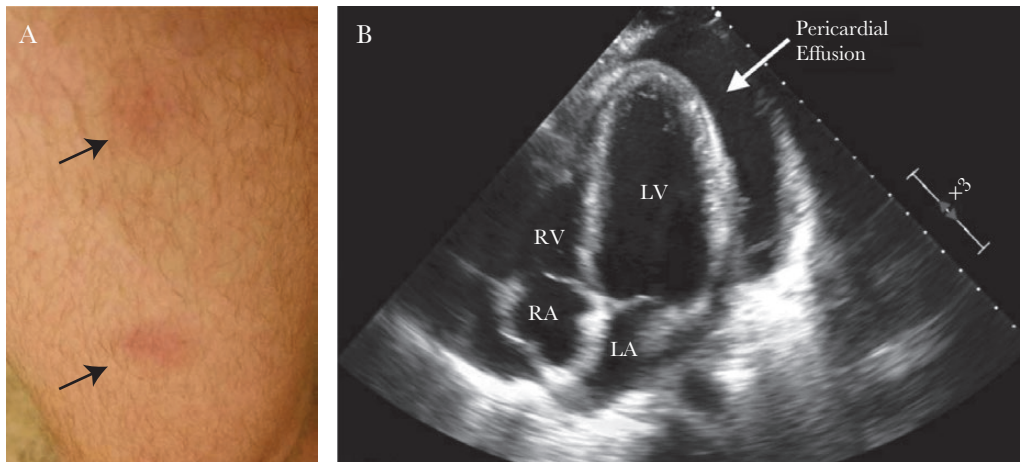


Figure 1. (A) Photo of the nodular rash (indicated by black arrows) on the left thigh. (B) Echocardiogram in the apical 4-chamber view showing a large circumferential pericardial effusion (indicated by a white arrow). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

less likely to have an immunocompromising condition such as chronic kidney disease, diabetes, or use of immune-modulating therapy [4]. The present case represents the first report of *H cinaedi* pericarditis complicated by cardiac tamponade.

Further work is needed to characterize the epidemiology and pathogenesis of *H cinaedi* infection. In the original prospective studies identifying *H cinaedi*, this bacterium was detected with increased frequency in HIV-negative MSM with proctitis relative to asymptomatic HIV-negative MSM, and it was not detected in any asymptomatic heterosexual individuals [1, 9]. Although these studies suggested a predilection for MSM, subsequent case reports and case series have not documented patient sexual orientation. The related pathogen *Campylobacter jejuni* is also thought to have the potential for transmission through anal sex and causes proctocolitis [10]. Although sexually transmitted infections and other sources of mucosal inflammation are thought to facilitate HIV transmission, additional

study of the relationship among *H cinaedi*, anal sex, the rectal microbiome, and HIV transmission risk is warranted [11].

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry can identify *H cinaedi* using the Bruker Biotyper RUO database, but the organism is not yet included in the US Food and Drug Administration-cleared database. Furthermore, commercial detection kits and biochemical detection methods have proven to be unreliable [12, 13]. Thus, 16S rRNA sequencing was used as an alternative method of identification.

Successful eradication of invasive *H cinaedi* infection often requires ≥ 4 weeks of therapy, and recurrences 2–10 weeks after completing therapy have been described in both immunocompetent and immunocompromised hosts [14–16]. Two studies have shown that *H cinaedi* is reliably susceptible in vitro to imipenem and minocycline and is variably susceptible to β -lactam antibiotics [13, 17]. In Japan,

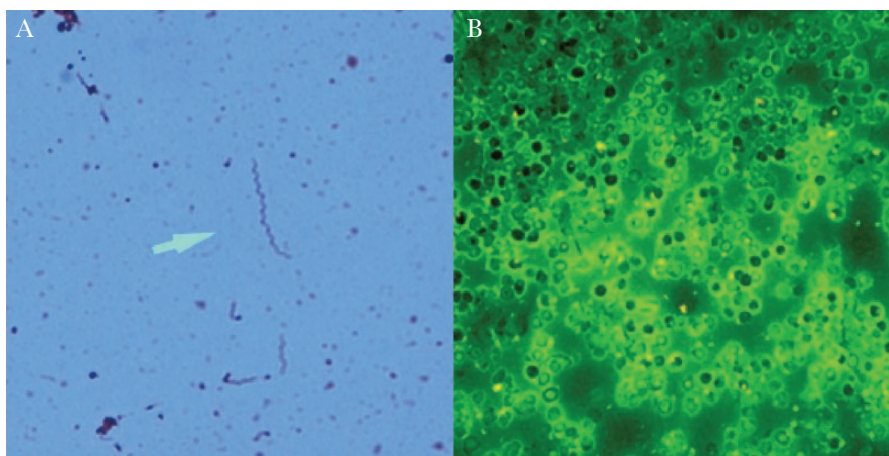


Figure 2. (A) Gram stain of the curved Gram-negative rod using carbol fuchsin as the counterstain and (B) acridine orange stain.

Table 1. Antibiotic Susceptibility Testing

| Antibiotic | Etest MIC (mcg/mL) |
|----------------------|--------------------|
| Penicillin | >256 |
| Ceftriaxone | 128 |
| Ampicillin/sulbactam | 64 |
| Azithromycin | >256 |
| Ciprofloxacin | >32 |
| Ertapenem | 0.25 |
| Meropenem | 0.032 |
| Gentamicin | 1 |
| Tetracycline | 1 |
| Doxycycline | 0.5 |

Abbreviations: MIC, minimum inhibitory concentration.

intrinsic mutations in the *gyrA* gene and 23S rRNA genes have resulted in increased *H cinaedi* resistance to fluoroquinolones and macrolides, respectively. To our knowledge, no reports of multidrug-resistant *H cinaedi* have been published; however, genomic studies have identified several putative efflux pumps [13]. Our patient improved on piperacillin/tazobactam, which was reported to be effective in an asplenic patient with *H cinaedi* bacteremia [18]. Further characterization of *H cinaedi* susceptibility patterns may be warranted to help guide empiric therapy in critically ill patients.

CONCLUSIONS

In summary, *H cinaedi* should be considered in patients presenting with fever and nodular rash, particularly in MSM, and disseminated disease may rarely present as cardiac tamponade.

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