



Helicobacter cinaedi bacteremia in a returning traveler

Andrew Fox-Lewis^{a,*}, Indira Basu^a, Anna Vesty^a, Gillian Henderson^a,
Aakash V. Chhibber^a, Mark Thomas^b

^a Microbiology Department, LabPLUS, Auckland City Hospital, Auckland, New Zealand

^b Infectious Diseases Department, Auckland City Hospital, Auckland, New Zealand

ARTICLE INFO

Article history:

Received 30 June 2020

Received in revised form 6 July 2020

Accepted 7 July 2020

Keywords:

Helicobacter

Helicobacter cinaedi

Fever in a returning traveler

Bacteremia

ABSTRACT

Of the non-*Helicobacter pylori* *Helicobacter* (NHPH) species, *Helicobacter cinaedi* is an emerging cause of infection in humans. Here we report a novel clinical presentation of *H. cinaedi* infection: a case of fever in a returning traveler. A 31 year old previously fit and well male presented with onset of fever 24 h after returning from travel in Singapore and Indonesia. Associated symptoms consisted of sore throat, mild shortness of breath, generalized myalgia and arthralgia, headache, and four episodes of loose stools. The patient recovered spontaneously without treatment and was discharged. After 4 days of incubation, blood cultures grew *H. cinaedi*. *H. cinaedi* is a slow-growing fastidious organism poorly detected by some commonly used automated blood culture systems, and difficult to identify using commercial or traditional biochemical identification systems. This case illustrates the importance of *H. cinaedi* as an emerging pathogen in immunocompetent patients, with a wide variety of possible clinical presentations. The challenges in the microbiological diagnosis of *H. cinaedi* infections lead us to speculate that *H. cinaedi* is an underdiagnosed cause of febrile illness, both in returning travelers and in other clinical settings. © 2020 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1 Introduction

The genus *Helicobacter* comprises 39 species, with *Helicobacter pylori* the most well-known pathogenic *Helicobacter* species in man [1]. Of the non-*Helicobacter pylori* *Helicobacter* (NHPH) species, *Helicobacter cinaedi* is an emerging cause of infection in humans [2]. Here we report a novel clinical presentation of *H. cinaedi* infection: a case of fever in a returning traveler.

2 Case history

A 31 year old previously fit and well male presented to the Emergency Department (ED) at Auckland City Hospital, New Zealand, with onset of fever 24 h after returning from 32 days of travel in Singapore and Indonesia. He had visited Singapore for five days, Indonesia (Bali) for six days, and Singapore again for 21 days, before returning directly to Auckland, New Zealand. He was asymptomatic during his travel. Approximately 24 h after arriving back in New Zealand he developed fever, sore throat, mild

shortness of breath without cough or coryza, generalized myalgia and arthralgia, intermittent left-sided headache, and four episodes of loose stools without nausea, vomiting or abdominal pain. He reported no animal exposure or ingestion of unclean water or undercooked food whilst travelling. The patient is a man-who-has-sex-with-men (MSM) and reported having multiple episodes of unprotected receptive/insertive anal intercourse during his travel.

On arrival in the ED he was febrile to 38.8 °C, with all other vital signs in the normal range and a normal physical examination with no rashes or cellulitis. Chest x-ray was normal, and urinary *Legionella pneumophila* and *Streptococcus pneumoniae* antigen tests were negative. He was found to have an elevated white cell count (16,450/μL) with neutrophilia (13,700/μL). Renal function and electrolytes were normal.

Based on his travel history and non-specific febrile illness, the patient met the clinical and epidemiological case definition for suspected coronavirus disease 2019 (COVID-19). Nasopharyngeal and oropharyngeal swabs tested negative for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and other respiratory viruses by polymerase chain reaction (PCR). Additionally, dengue, chikungunya and zika viruses were not detected on whole blood PCR, and feces PCR did not detect any bacterial, viral or parasitic gastrointestinal pathogens. Tests for human immunodeficiency virus and *Treponema pallidum* infection were also negative. The patient was hospitalized for one day for observation. During

* Corresponding author at: Postal address: Microbiology Department, LabPLUS, Building 31, Auckland City Hospital, Gate 4 off Grafton Rd, Grafton, Auckland, New Zealand.

E-mail address: afoxlewis@gmail.com (A. Fox-Lewis).

this time his fever defervesced and his symptoms fully resolved without treatment, and he was discharged.

At the time of discharge from hospital, two sets of blood cultures were negative. After 4 days of incubation the aerobic bottle in one set flagged positive. Tiny Gram-negative "seagull" shaped (helical/spiral shaped) bacilli, with an appearance similar to *Campylobacter* species, were seen on Gram-stain. Subcultures were set up on sheep blood agar (SBA) incubated in micro-aerophilic (microaerobic) conditions at 37 °C and 42 °C, and also on brain heart infusion (BHI) agar incubated anaerobically. On day 8, several small grey oxidase-positive colonies were observed on the SBA plate incubated at 37 °C, and a single colony on the anaerobic BHI plate. Matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) analysis failed to identify the organism and it was sent for 16S rRNA gene sequencing. Analysis of the V1-V3 region of the 16S rRNA gene revealed 100 % sequence similarity with *Helicobacter cinaedi* species, confirming the patient's presentation had been due to *H. cinaedi* infection.

3 Discussion

The *Helicobacter* species can be divided into gastric (stomach) and enterohepatic (intestine and hepatobiliary) groups [3]. Within the gastric group, the key human pathogen is *H. pylori*. Species belonging to the enterohepatic group inhabit the gastrointestinal and hepatobiliary systems of various mammal and bird hosts [3]. One of the most studied enterohepatic *Helicobacter* species is *Helicobacter cinaedi*, which is being increasingly demonstrated as a cause of human infection [2]. *H. cinaedi* was first isolated from rectal swabs from MSM with gastroenteritis, proctocolitis and proctitis in 1984 [1]. At this time it was designated as *Campylobacter*-like organism type-1 (CLO-1), and was later re-classified as *H. cinaedi* in 1991 [1]. Since this time human infection with *H. cinaedi* has been increasingly documented in other patient groups, including both immunocompromised and immunocompetent hosts, with a variety of clinical presentations and syndromes [1,2]. Bacteremia is one of the most common manifestations of *H. cinaedi* infection, and is thought to be due to bacterial translocation from the intestinal tract to the vascular system [1,4].

Here we report a case of fever in a returning traveler due to *H. cinaedi* infection, as evidenced by *H. cinaedi* isolated from blood culture. As far as the authors are aware, *H. cinaedi* has not previously been linked to the syndrome of fever in a returning traveler, and thus this represents a novel clinical presentation for this organism. Following the patient's return he reported a few episodes of loose stools, which could indicate possible mild gastroenteritis or proctocolitis. Given that *H. cinaedi* was first identified in MSM with gastrointestinal symptoms, and has a propensity for gastrointestinal translocation into the blood stream, we postulate that sexual transmission led to *H. cinaedi* gastrointestinal infection and subsequent bacteremia, manifesting as a non-specific febrile illness in a returning traveler and clinical suspicion of COVID-19.

This case further illustrates the importance of *H. cinaedi* as an emerging pathogen in immunocompetent patients, with a wide

variety of possible clinical presentations [1,2]. As a slow-growing fastidious organism, *H. cinaedi* is difficult to isolate from culture [1]. Indeed, the time for blood cultures to become positive for *H. cinaedi* can be greater than five days for 45 % of isolates, indicating nearly half of *H. cinaedi* bacteremias will be missed by laboratories where blood cultures are incubated for up to five days [5]. Additionally, *H. cinaedi* is poorly detected by some commonly used automated blood culture systems (e.g. BacT/Alert System) [6]. To compound these detection issues, once successfully cultured *H. cinaedi* cannot be reliably identified by commercial biochemical identification systems (e.g. Vitek 2) or traditional biochemical methods [4]. Given these factors, the microbiological diagnosis of *H. cinaedi* infections is extremely challenging for the clinical microbiology laboratory. These manifold diagnostic challenges lead us to speculate that *H. cinaedi* is an underdiagnosed cause of febrile illness, both in returning travelers such as in the case reported here, and in other clinical settings.

Consent

Informed consent was obtained from the patient for the publication of this clinical case report.

Author contributions

MT was the attending physician. AFL collated the clinical and laboratory data. IB, AV, GH and AVC conducted the laboratory work involved in isolating and identifying the organism. AFL, IB, AV, GH, AVC and MT wrote the manuscript.

Funding

The authors received no specific funding for this work.

Declaration of Competing Interest

All authors declare no conflict of interests.

References

- [1] Kawamura Y, Tomida J, Morita Y, et al. Clinical and bacteriological characteristics of *Helicobacter cinaedi* infection. *J Infect Chemother* 2014;20(9):517–26 doi:10.1016/j.jiac.2014.06.007. Epub 2014 Jul 9. Review..
- [2] Ménard A, Smet A. Review: other *Helicobacter* species. *Helicobacter* 2019;24 (Suppl 1):e12645, doi:http://dx.doi.org/10.1111/hel.12645.
- [3] Carroll KC, Pfaller MA, Landry ML, et al. Manual of clinical microbiology. 12th edition American Society for Microbiology; 2019 Chapter 59 – *Helicobacter*:1044–1057.
- [4] Bateman AC, Butler-Wu SM. The brief case: bacteremia caused by *Helicobacter cinaedi*. *J Clin Microbiol* 2016;55(1):5–9, doi:http://dx.doi.org/10.1128/JCM.02936-15 Print 2017 Jan.
- [5] Araoka H, Baba M, Kimura M, et al. Clinical characteristics of bacteremia caused by *Helicobacter cinaedi* and time required for blood cultures to become positive. *J Clin Microbiol* 2014;52(5):1519–22 doi: 10.1128/JCM.00265-14. Epub 2014 Feb 26. Erratum in: *J Clin Microbiol*. 2014 Jul;52(7):2745..
- [6] Miyake N, Chong Y, Nishida R, et al. A dramatic increase in the positive blood culture rates of *Helicobacter cinaedi*: the evidence of differential detection abilities between the Bactec and BacT/Alert systems. *Diagn Microbiol Infect Dis* 2015;83(3):232–3 doi: 10.1016/j.diagmicrobio.2015.07.017. Epub 2015 Jul 26..