Title
Chronic \textit{Helicobacter cinaedi} cellulitis diagnosed by microbial polymerase chain reaction.

Permalink
https://escholarship.org/uc/item/9mr9s1c5

Journal
JAAD case reports, 3(5)

ISSN
2352-5126

Authors
Matsumoto, Andrew
Yeh, Iwei
Schwartz, Brian
\textit{et al.}

Publication Date
2017-09-01

DOI
10.1016/j.jdcr.2017.05.009

Peer reviewed
**CASE REPORT**

**Chronic *Helicobacter cinaedi* cellulitis diagnosed by microbial polymerase chain reaction**

Andrew Matsumoto, BS, Iwei Yeh, MD, PhD, Brian Schwartz, MD, Michael Rosenblum, MD, PhD, and Timothy H. Schmidt, MD, PhD
San Francisco, California and Albany, New York

**Key words:** 16S rRNA; chronic cellulitis; granulomatous and suppurative dermatitis; *Helicobacter cinaedi*; multiple abscesses; primary humoral immunodeficiency; universal microbial polymerase chain reaction; X-linked agammaglobulinemia.

**INTRODUCTION**

*Helicobacter cinaedi* is an unusual cause of cellulitis in immunocompromised patients. The organism is fastidious, and blood cultures are often negative, making the diagnosis challenging, especially in those without systemic signs. We report a case of chronic *H. cinaedi* cellulitis in a patient with X-linked agammaglobulinemia (XLA) diagnosed by universal microbial polymerase chain reaction (PCR).

**CASE REPORT**

A 48-year-old man with XLA presented to an outside clinic with chronic leg lesions. He had been treated with intravenous immunoglobulin since 1974. Painful, bruiselike lesions developed below his knees 5 to 6 months before presentation. He also reported fatigue, inguinal discomfort, joint pain, and shortness of breath concomitant with worsening of his leg lesions. The lesions were initially thought to be clinically consistent with erythema nodosum, and he was started on prednisone, 20 mg daily. After a few weeks of treatment there was limited improvement, so he was referred to the dermatology clinic for evaluation.

On examination, he had normal vital signs and appeared in no acute distress. Skin examination found scattered, variably erythematous, violaceous, hyperpigmented, and firm plaques on the distal legs that were several centimeters in diameter, some with overlying superficial desquamation (Fig 1). Our differential diagnoses included infection (including atypical bacterial and fungal), erythema nodosum, erythema induratum, Sweet syndrome, and primary cutaneous granulomas as a manifestation of immunodeficiency. Laboratory evaluation found a mild transaminitis, white blood cell count of 11.4×10⁹/L (absolute neutrophil count of 10.7, absolute lymphocyte count of 0.3, and CD4 count of 154 cells/mm³), IgM and IgA below the measurable range, IgG in the normal range, C-reactive protein of 130 mg/L, erythrocyte sedimentation rate of 82 mm/h, procalcitonin of 0.75 ng/mL, and a negative interferon-γ release assay (QuantiFERON, QIAGEN, Hilden, Germany). During the course of his evaluation, 3 punch biopsies found granulomatous and suppurative dermatitis with lipomembranous fat necrosis (Fig 2). Periodic acid–Schiff–diastase, Brown-Brenn, and Fite stains were negative for fungi, bacteria, and acid-fast bacilli, respectively. Multiple cultures of the biopsied skin for bacteria, fungi, and mycobacteria were negative as well. During this time, he was evaluated by the urology department for orchalgia and epididymitis was diagnosed. He

---

From the Departments of Dermatology, Pathology, and Infectious Disease, University of California, San Francisco and Albany Medical College. Funding sources: None. Conflicts of interest: None declared. Correspondence to: Timothy H. Schmidt, MD, PhD, UCSF Department of Dermatology 1701 Divisadero Street, 3rd Floor, San Francisco, CA 94115. E-mail: timothy.hunter.schmidt@gmail.com.

JAAD Case Reports 2017;3:398-400. 2352-5126 © 2017 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). http://dx.doi.org/10.1016/j.jdcr.2017.05.009
was started on trimethoprim-sulfamethoxazole (TMP-SMX), 160 mg to 800 mg twice a day for 6 weeks and then daily for prevention. Treatment with TMP-SMX improved his orchalgia but did not improve his rash. As his prednisone was tapered down, the rash spread further, and tender, violaceous, mobile, subcutaneous nodules developed on his trunk.

Although stains and cultures were negative, the patient’s symptoms, immunodeficiency, and pathology suggested infection. The infectious disease department was consulted and recommended...
sending tissue from a skin biopsy for universal microbial PCR. This PCR used a 16S rRNA primer set to identify bacteria in addition to other primer sets for mycobacteria and fungi. An amplified PCR product from leg skin was sequenced and identified as coming from \textit{H. cinaedi}. To confirm the diagnosis, one of the recently appeared, subcutaneous nodules from the patient’s trunk was excised and sent for pathology, culture, and repeat microbial PCR. The pathology findings showed a neutrophilic abscess with fat necrosis. Bacterial PCR was once again positive for \textit{H. cinaedi}. Blood cultures obtained while the patient was on TMP-SMX were incubated for 6 days but were negative. The patient was started on doxycycline, 100 mg twice a day, in addition to TMP-SMX. There was significant improvement in his rash and fatigue 3 weeks later. After 4 months, his systemic symptoms had completely resolved, and his rash had resolved to hyperpigmentation and mild atrophy so all antibiotics were stopped.

**DISCUSSION**

\textit{H. cinaedi} is a gram-negative enteric curved (helix-shaped) bacillus that causes gastroenteritis, bacteremia, and rash, usually in immunocompromised patients. Patients typically appear acutely ill and are found to have fever and bacteremia. According to a retrospective review of 73 mostly immunocompromised patients with \textit{H. cinaedi} bacteremia, skin lesions occur in 30\% of patients and appear as erythematous patches and plaques on the extremities.\footnote{Shimizu S, Shimizu H. Cutaneous manifestations of Helicobacter cinaedi infection and the usefulness of gene analysis of isolated bacteria}. Skin biopsy often finds a mixed inflammatory infiltrate in the dermis and subcutis. Diagnosis is very difficult by traditional culture techniques. The authors of the previously mentioned study examined tissue culture and bacterial stains of skin lesions of 6 patients with \textit{H. cinaedi} bacteremia, and all were found to be negative.\footnote{Harp J, Coggshall K, Ruben BS, Ramirez-Valle F, He SY, Berger TG. Cutaneous granulomas in the setting of primary immunodeficiency: a report of four cases and review of the literature. \textit{Int J Dermatol.} 2015;54(6):617-625.} Correct diagnosis requires a high index of suspicion and microbiologic confirmation. \textit{H. cinaedi} infections generally respond to extended courses of penicillins, carbapenems, aminoglycosides, or tetracyclines.\footnote{Uckay I, Garbino J, Dietrich PY, Ninet B, Rohner P, Jacomo V. Recurrent bacteremia with Helicobacter cinaedi: case report and review of the literature. \textit{BMC Infect Dis.} 2006;6:86.} The lack of response of our patient’s rash to TMP-SMX prescribed for epididymitis is in line with documented resistance of \textit{H. cinaedi} to that antibiotic.\footnote{Shimizu T, Choi E, Petersen CP, et al. Characterization of progressive metaplasia in the gastric corpus mucosa of Mongolian gerbils infected with Helicobacter pylori. \textit{J Pathol.} 2016;239(4):399-410.}

Recognition of \textit{H. cinaedi} infection in our case was delayed because the bacterium was not detected by routine stains or cultures, consistent with current literature in which cultures are often negative.\footnote{Harp J, Coggshall K, Ruben BS, Ramirez-Valle F, He SY, Berger TG. Cutaneous granulomas in the setting of primary immunodeficiency: a report of four cases and review of the literature. \textit{Int J Dermatol.} 2015;54(6):617-625.} One possibility is that our patient’s immunodeficiency allowed for indolent infection and bacteremia (as demonstrated by the late onset of bacteria-positive abscesses at distant sites) without fever or positive blood culture. Indeed, a case of afebrile but ulcerating \textit{H. cinaedi} skin infection has been reported in a patient with XLA.\footnote{Uckay I, Garbino J, Dietrich PY, Ninet B, Rohner P, Jacomo V. Recurrent bacteremia with Helicobacter cinaedi: case report and review of the literature. \textit{BMC Infect Dis.} 2006;6:86.} This patient had an evolving rash for 5 years before it formed a pyoderma gangrenosum—like ulcer, and \textit{H. cinaedi} was detected via PCR of the skin. Similarly, another case of a afebrile patient with XLA who had hyperpigmented macules, whom later was found to have positive blood cultures and PCR findings for \textit{H. cinaedi}, has been reported.\footnote{Dua J, Elliot E, Bright P, et al. Pyoderma gangrenosum-like ulcer caused by Helicobacter cinaedi in a patient with x-linked agammaglobulinemia. \textit{Clin Exp Dermatol.} 2012;37(6):642-645.} PCR has also been used to detect the bacterium in the blood, urine, and stool of infected hospital patients.\footnote{Simons E, Spacek LA, Lederman HM, Winkelstein JA. Helicobacter cinaedi bacteremia presenting as macules in an afebrile patient with X-linked agammaglobulinemia. \textit{Infection.} 2004;32(6):367-368.} These observations suggest that PCR may be the best test to rule out \textit{H. cinaedi} infection, which can mimic other illnesses and avoid detection by other means. Before PCR was available, it is conceivable that similar cases of indolent infections like this one went misdiagnosed from lack of a sufficiently sensitive microbiologic test.

**REFERENCES**

1. Shimizu T, Choi E, Petersen CP, et al. Characterization of progressive metaplasia in the gastric corpus mucosa of Mongolian gerbils infected with Helicobacter pylori. \textit{J Pathol.} 2016;239(4):399-410.
2. Harp J, Coggshall K, Ruben BS, Ramirez-Valle F, He SY, Berger TG. Cutaneous granulomas in the setting of primary immunodeficiency: a report of four cases and review of the literature. \textit{Int J Dermatol.} 2015;54(6):617-625.
3. Shimizu S, Shimizu H. Cutaneous manifestations of Helicobacter cinaedi infection and the usefulness of gene analysis of isolated bacteria. \textit{J Pathol.} 2012;239(4):399-410.
4. Uckay I, Garbino J, Dietrich PY, Ninet B, Rohner P, Jacomo V. Recurrent bacteremia with Helicobacter cinaedi: case report and review of the literature. \textit{BMC Infect Dis.} 2006;6:86.
5. Dua J, Elliot E, Bright P, et al. Pyoderma gangrenosum-like ulcer caused by Helicobacter cinaedi in a patient with x-linked agammaglobulinemia. \textit{Clin Exp Dermatol.} 2012;37(6):642-645.
6. Simons E, Spacek LA, Lederman HM, Winkelstein JA. Helicobacter cinaedi bacteremia presenting as macules in an afebrile patient with X-linked agammaglobulinemia. \textit{Infection.} 2004;32(6):367-368.
7. Oyama K, Khan S, Okamoto T, et al. Identification of and screening for human Helicobacter cinaedi infections and carriers via nested PCR. \textit{J Clin Microbiol.} 2012;50(12):3893-3900.
8. Sasahara Y, Noguchi S, Orihashi T, et al. [Three cases of bacteremia due to Helicobacter cinaedi infection and the usefulness of gene analysis of isolated bacteria]. \textit{J UOEH.} 2015;37(4):293-298.