

Generalized Lymphadenopathy due to *Tropheryma whipplei*

Krüger, Stig Ree; Norvard, Espen Rigby; Larssen, Kjersti Wik; Maierhofer, Ursa; Hestmann, Helene; Papathomas, Thomas

DOI:

[10.1016/j.ijid.2024.107033](https://doi.org/10.1016/j.ijid.2024.107033)

License:

Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

Document Version

Publisher's PDF, also known as Version of record

Citation for published version (Harvard):

Krüger, SR, Norvard, ER, Larssen, KW, Maierhofer, U, Hestmann, H & Papathomas, T 2024, 'Generalized Lymphadenopathy due to *Tropheryma whipplei*: Thinking outside the box!', *International Journal of Infectious Diseases*, vol. 143, 107033. <https://doi.org/10.1016/j.ijid.2024.107033>

[Link to publication on Research at Birmingham portal](#)

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.



Medical Imagery

Generalized lymphadenopathy due to *Tropheryma whipplei*: Thinking outside the box!

Stig Ree Krüger^{1,*}, Espen Rigby Norvard¹, Kjersti Wik Larssen², Ursa Maierhofer¹, Helene Hestmann³, Thomas Papathomas^{1,4}

¹ Department of Clinical Pathology, Vestre Viken Hospital Trust, Drammen, Norway

² Department of Medical Microbiology, St. Olav's University Hospital, Trondheim, Norway

³ Department of Medicine, Vestre Viken Hospital Trust, Bærum, Norway

⁴ Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom

ARTICLE INFO

Article history:

Received 21 February 2024

Revised 26 March 2024

Accepted 27 March 2024

Keywords:

Whipple's disease

Tropheryma whipplei

Generalized lymphadenopathy

PCR analysis

Case presentation

A 58-year-old male with no travel history was admitted to the medical emergency department with a 6-month history of weight loss, pruritus, and reduced appetite, deteriorating with one week of loose stools and nausea. Blood tests indicated a slightly elevated C-reactive protein as well as low-grade anemia, eosinophilia, and hyponatremia. A computed tomography (CT) scan of the abdomen (Figure 1a) revealed generalized lymphadenopathy. A lymph node biopsy displayed granulomatoid accumulations of variably foamy macrophages containing Periodic acid-Schiff (PAS)- and Grocott methenamine silver (GMS)-positive rods (Figure 1b-d). A positive in-house polymerase chain reaction (PCR) targeting *T. whipplei*-deoxyribonucleic acid (DNA) (Heat shock protein and 16S ribosomal ribonucleic acid [RNA] genes) on both lymph node and small intestine biopsies confirmed the diagnosis of Whipple's

disease. The patient was discharged with improving symptoms after 1 week's treatment with Ceftriaxone and is planned for 1-year combination therapy with oral Doxycycline and Plaquenil [1].

Whipple's disease is a systemic infection caused by the Gram-positive bacterium *T. whipplei*. Symptoms are classically unspecific including digestive disorders and a longer history of intermittent and migrating arthralgia, but atypical forms are not unusual [1,2]. The gold standard of diagnosing classic Whipple's disease is based on small bowel biopsies. However, a high index of suspicion should be kept also for other site-specific biopsies exhibiting comparable morphology and histochemical findings [3]. *T. whipplei*-specific immunohistochemistry is available [4], while PCR on target tissue(s) or body fluid(s) of relevance is utilized to establish the diagnosis. Histopathologists should be aware of histochemical and immunohistochemical limitations [5] and include PCR testing in the diagnostic armamentarium.

* Corresponding author: Tel.: +47 32 80 38 24

E-mail address: stig.ree.kruger@vestreviken.no (S.R. Krüger).

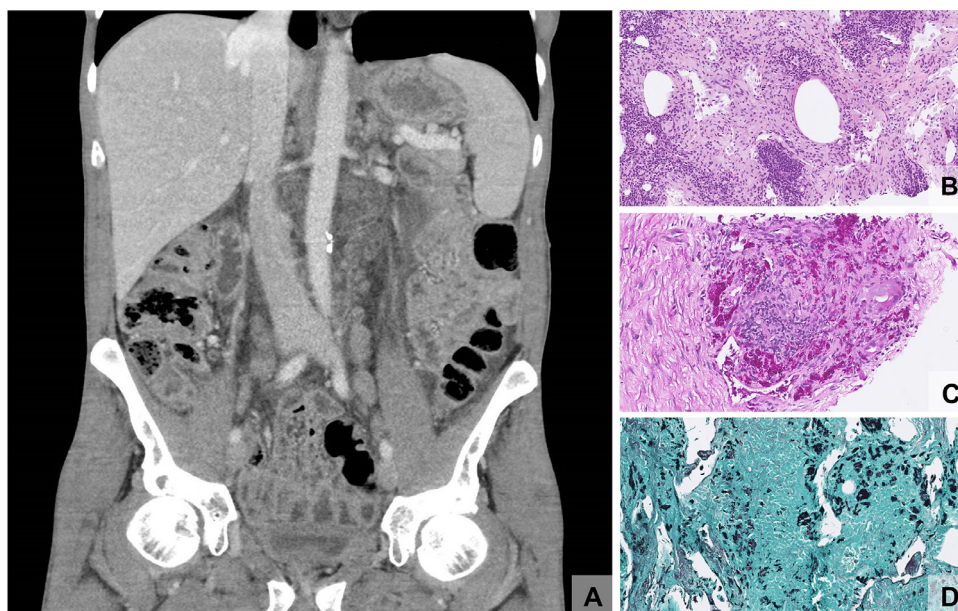


Figure 1. (a) Computed tomography image (coronal plane) showing extensive periaortic lymphadenopathy with various densities. (b) Haematoxylin and eosin (H&E) stained needle biopsy from mesenteric lymph node displaying dense collections of foamy macrophages containing (c) Periodic acid-Schiff (PAS) positive inclusions and (d) Grocott methenamine silver (GMS) positive rods; Giemsa and Ziehl-Neelsen stains were unremarkable (images not shown). H&E (x 24 magnification), PAS (x 40 magnification), and GMS (x 40 magnification); Digital slides | Whole Slide Imaging - WSI | Hamamatsu Photonics.

Declaration of competing interest

The authors have no competing interests to declare.

Funding

This research did not receive any specific grant from funding agencies in the public or not-for-profit sectors.

Ethical approval

A written informed consent was obtained from the patient.

Author contributions

Stig Ree Krüger drafted the manuscript. Stig Ree Krüger, Urs Maierhofer, and Thomas Papatomas reviewed radiological and histopathological images and prepared the figure. Thomas Papatomas conceptualized and supervised the project and revised the

first and final drafts of the manuscript. Helene Hestmann, Espen Rigby Norvard, and Kjersti Wik Larssen were involved in diagnosis and patient care. All authors critically revised, read, and approved the manuscript.

References

- [1] Dolmans RAV, Boel CHE, Lacle MM, Kusters JG. Clinical manifestations, treatment, and diagnosis of *Tropheryma whippelii* infections. *Clin Microbiol Rev* 2017;**30**:529–55. doi:[10.1128/CMR.00033-16](https://doi.org/10.1128/CMR.00033-16).
- [2] Lagier JC, Raoult D. Whipple's disease and *Tropheryma whippelii* infections: when to suspect them and how to diagnose and treat them. *Curr Opin Infect Dis* 2018;**31**:463–70. doi:[10.1097/QCO.0000000000000489](https://doi.org/10.1097/QCO.0000000000000489).
- [3] Boumaza A, Ben Azzouz E, Arrindell J, Lepidi H, Mezouar S, Desnues B. Whipple's disease and *Tropheryma whippelii* infections: from bench to bedside. *Lancet Infect Dis* 2022;**22**:e280–91. doi:[10.1016/S1473-3099\(22\)00128-1](https://doi.org/10.1016/S1473-3099(22)00128-1).
- [4] Crews NR, Cawcutt KA, Pritt BS, Patel R, Virk A. Diagnostic approach for classic compared with localized Whipple disease. *Open Forum Infect Dis* 2018;**5**:ofy136. doi:[10.1093/ofid/ofy136](https://doi.org/10.1093/ofid/ofy136).
- [5] Wartique L, Lagier JC, Raoult D, Jamilloux Y, Sève P. Mesenteric lymphadenitis as a presenting feature of Whipple's disease: value of PCR analysis. *Int J Infect Dis* 2018;**75**:15–17. doi:[10.1016/j.ijid.2018.08.003](https://doi.org/10.1016/j.ijid.2018.08.003).