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Medical Imagery

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

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## 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 Whippleś 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.

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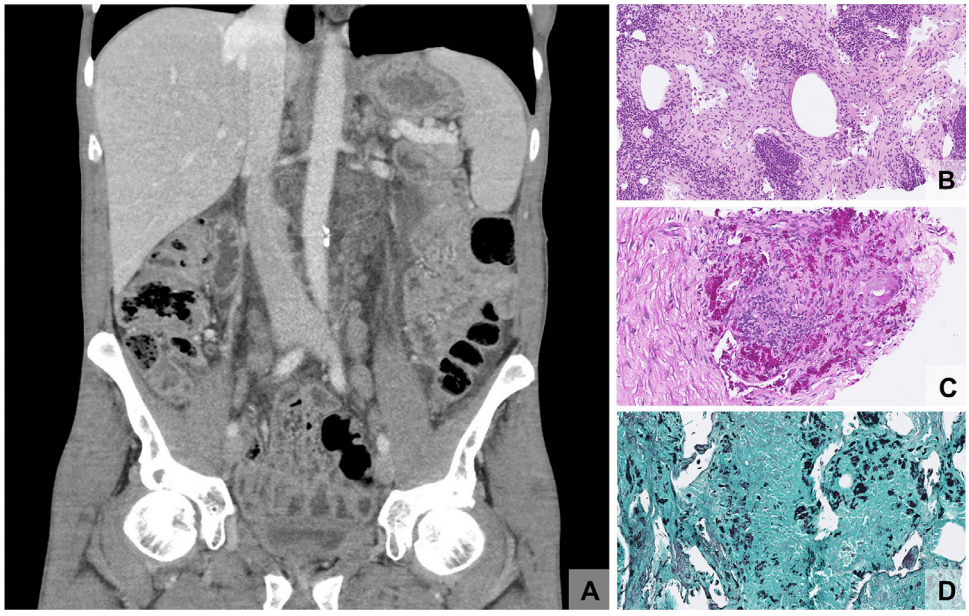


**Figure 1.** (a) Computed tomography image (coronal plane) showing extensive periaortic lymphadenopathy with various densities. (b) Haematoxylin and eosin (H&E) stained needle biopsy from mesenteric lymph node displaying dense collections of foamy macrophages containing (c) Periodic acid-Schiff (PAS) 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.

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## Ethical approval

A written informed consent was obtained from the patient.

## Author contributions

Stig Ree Krüger drafted the manuscript. Stig Ree Krüger, Ursa Maierhofer, and Thomas Papathomas reviewed radiological and histopathological images and prepared the figure. Thomas Papathomas 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.

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