

An unusual presentation of *Tropheryma whipplei* infection

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Whipple's disease is an infection caused by the Gram-positive bacillus *Tropheryma whipplei*. Invasion or uptake of the bacteria can occur in various parts of the body. The differential diagnoses are broad due to the wide spectrum of infection, and the disease is diagnosed based on biopsy of suspected lesions, usually in the small intestine. We present the case of a 56-year-old man with no significant prior medical history who presented with swelling and pain in the left eye. Review of systems revealed 6 months of persistent diarrhea, and intestinal biopsy revealed periodic acid-Schiff–positive macrophages.

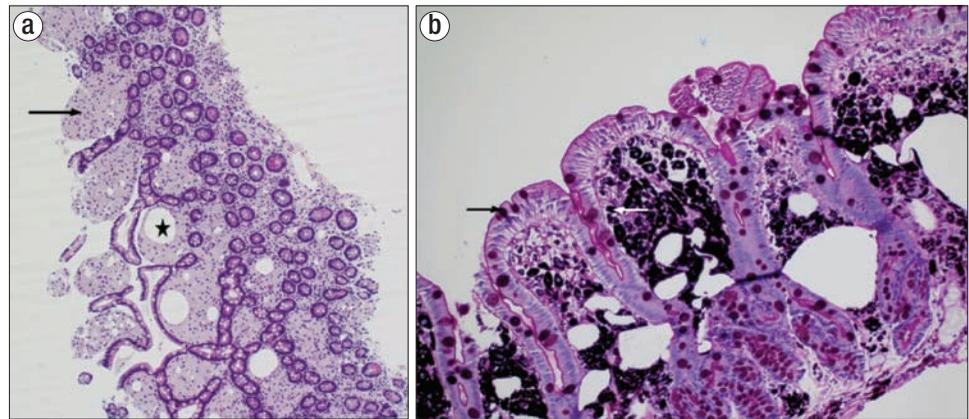


Figure 1. Small bowel biopsy showing (a) blunted villi and expansion with periodic acid-Schiff–positive macrophages (arrow) and lipid droplets (star) (100 \times); and (b) mucin in goblet cells (black arrow) and macrophages with periodic acid-Schiff–resistant material (white arrow) (400 \times).

Whipple's disease was identified in the early 1900s, but it was not cultured until 1997 (1). It is caused by *Tropheryma whipplei*, a Gram-positive bacillus that is related to actinomycetes and is fairly ubiquitous in nature with a wide spectrum for infection, including the intestinal epithelium, macrophages, capillary and lymphatic endothelium, colon, liver, brain, heart, lung, synovium, kidney, bone marrow, and skin (2). Due to the infection's widespread involvement, clinical manifestations are broad but most commonly include arthralgia, weight loss, diarrhea, and abdominal pain. The incidence of Whipple's disease is low; this case featured an unusual presentation.

CASE REPORT

A 56-year-old man with no significant prior medical history presented with swelling and pain in the left eye. He was found to have a complicated pseudomonas infection involving the periorbit and sinuses as well as bilateral pneumonia with cavitary disease. For 6 months, he had endured persistent diarrhea, night sweats, fatigue, a 60-pound weight loss, and hyperpigmentation of the skin. Upper endoscopy showed gastritis but no masses or bleeding ulcers. Small bowel biopsies were obtained, and histologic evaluation demonstrated small intestinal mucosa with villous blunting and expansion with periodic

acid-Schiff–positive macrophages within the lamina propria (Figure 1). Whipple's polymerase chain reaction (PCR) was obtained but returned negative results. Treatment for Whipple's disease was initiated with doxycycline and hydroxychloroquine. The patient demonstrated complete remission of his symptoms.

DISCUSSION

The annual incidence of Whipple's disease is approximately 1 per 1,000,000 people (3). In general, it is noted to have two distinct stages. The first stage is a prodromal stage consisting of nonspecific findings such as arthralgias, adenopathy, and fever. The second stage is the steady-state stage consisting of organ-specific findings such as diarrhea, weight loss, and neurological symptoms. The typical time course from onset of the prodromal stage to the steady-state stage is thought to be around 6 years, but it can be triggered much more quickly in certain situations such as an immunocompromised host (2).

The current methods for diagnosis are culture, serology, pathology (i.e., duodenal biopsy), and molecular testing. Data

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have shown that use of PCR techniques on intestinal biopsies is not necessary to confirm the diagnosis. Additionally, PCR tests risk contamination by environmental DNA, lack visual controls, and are difficult to perform on paraffin sections (4). In this case, the diagnosis was confirmed with periodic acid-Schiff staining of duodenal biopsies as well as villous atrophy. Though the Whipple's PCR test was negative, small bowel histology was determined to be pathognomonic for Whipple's disease. A dramatic response to targeted therapy further confirmed the diagnosis.

Without treatment, Whipple's disease can be fatal and even with treatment relapse can occur. This case illustrates

the importance of clinical suspicion driving a diagnosis and indicates that current diagnostic methods for Whipple's disease may be limited.

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