

## Case Report

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# A typical presentation of Whipple's disease: A case report challenging the classic triad

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## Introduction

Whipple's Disease (WD) is a chronic, systemic, relapsing infection caused by *Tropheryma whipplei*, an actinobacterium found widely in the environment. It is a rare condition, with a prevalence of 1-3 per 1,000,000, predominantly affecting middle-aged Caucasian men [1,2]. On average, patients are diagnosed at around 55 years of age, and approximately 85% of cases occur in males [3]. The disease presents with a broad spectrum of symptoms. In fact, the classic triad of diarrhea, weight loss, and arthralgias is well-documented; however atypical presentations can confound diagnosis, which leads to a real diagnostic challenge [4].

Herein we report a case of a 64-year-old male patient presenting with chronic gastrointestinal symptoms and signs of malabsorption. This report contributes to the understanding of WD's variable clinical presentations and emphasizes the need for maintaining a high index of suspicion for the disease in patients with unexplained chronic gastrointestinal complaints.

## Abstract

Whipple's Disease (WD) is a rare, potentially life-threatening infection caused by *Tropheryma whipplei*, characterized by a diverse array of symptoms that complicate diagnosis. We present a case of a 64-year-old male with chronic gastrointestinal symptoms, predominantly abdominal pain and watery diarrhea, who notably lacked the classical arthralgias associated with WD. Histopathological examination of duodenal biopsies revealed PAS-positive macrophages, confirming the diagnosis. The patient was treated with a standard antibiotic regimen, resulting in significant clinical improvement and complete symptom resolution. This case underscores the diagnostic complexities of WD and emphasizes the necessity for a high index of suspicion even in atypical presentations. Adherence to established treatment protocols is essential for achieving optimal patient outcomes.

## Case presentation

A 64-year-old man presented with a six-month history of progressive weight loss, fatigue, abdominal pain, nausea, and watery diarrhea. He reported no prior medical history, surgeries, or relevant travel history. Physical examination showed that he was conscious and cooperative but cachectic in appearance. The patient was afebrile and did not have palpable nodules or joint changes. Laboratory workup revealed iron deficiency anemia (Hemoglobin 8.2 g/dL, ferritin 10 ng/mL) and hypoalbuminemia (28 g/dL) hypocholesterolemia (2 g/L). He did not have leukocytosis ( $6.5 \times 10^9/L$ ) or neutrophilia ( $4.7 \times 10^9/L$ ). Inflammatory markers were elevated (C-reactive protein and erythrocyte sedimentation at 20 mg/dL and 90 mm, respectively). Serologic and stool evaluations for common infectious etiologies were negative. Celiac disease serology was also negative. Abdominal Computed Tomography (CT) demonstrated mesenteric lymphadenopathy.

Esophagogastroduodenoscopy (EGD) showed thickened duodenal folds with whitish plaques diffusely distributed in the distal duodenum, while colonoscopy yielded normal results. Duodenal biopsies revealed PAS-positive macrophages in the lamina propria (Figures 1 & 2), confirming the diagnosis of WD.

The patient received intravenous ceftriaxone at a dosage of 2 g per day for two weeks, followed by a year-long course of oral trimethoprim (160 mg) and sulfamethoxazole (800 mg) taken twice daily. The patient began to show significant improvement within two weeks of starting the treatment and eventually experienced complete resolution of symptoms during a 12-month follow-up period.

### Discussion

Whipple's disease remains a rare but clinically significant condition characterized by its multisystemic involvement and diagnostic challenges. In this case report, the patient primarily presented with gastrointestinal symptoms including abdominal pain and chronic diarrhea, which are classic symptoms of WD. The absence of arthralgias in our case underscores the limitations of relying solely on the classic triad for diagnosis. Previous reports support this observation. For example, Khrais et al. described a 67-year-old immunocompromised patient with HIV and WD who also lacked arthralgias [5]. Similarly, Kutlua et al. (2021) documented a case where WD manifested only with diarrhea and malabsorption, aligning with the gastrointestinal-focused presentation observed in our patient [6].

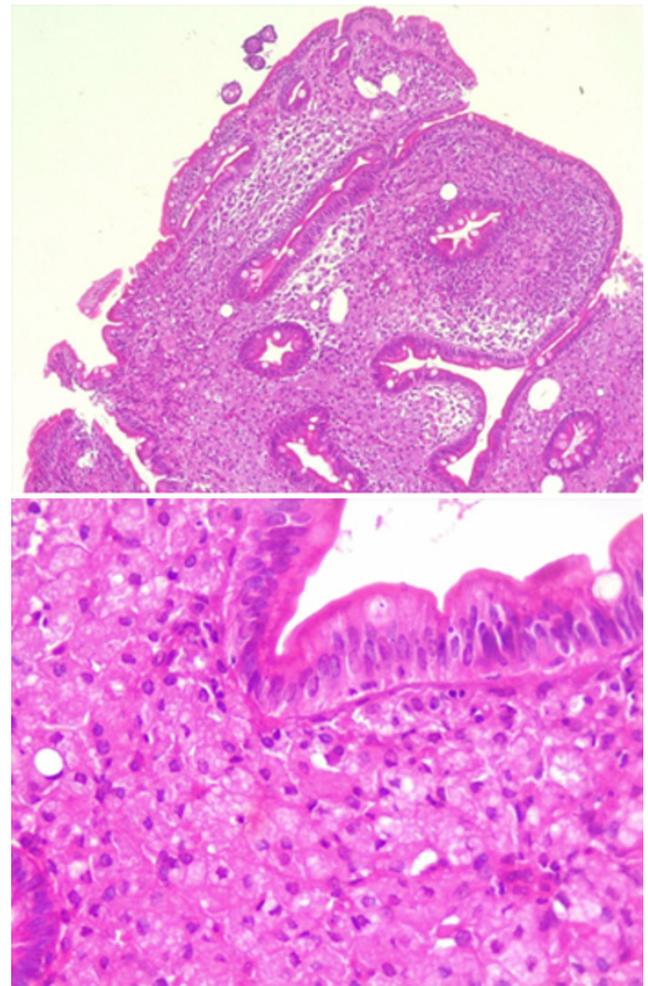
Thus, WD, although rare, should be considered as a potential diagnosis for abdominal pain and chronic diarrhea due to its potentially fatal outcome if untreated [7,8].

Given its potential for severe complications if left untreated, WD should be considered in the differential diagnosis for patients presenting with chronic abdominal pain and diarrhea, even in the absence of the complete symptom triad [7,8]. While our patient did not show systemic organ involvement, it is important to recognize that WD can also present with neurological, ophthalmologic, pulmonary, cardiac, or hematologic manifestations. Such systemic involvement necessitates prompt diagnosis and treatment to prevent serious outcomes [7,9,10].

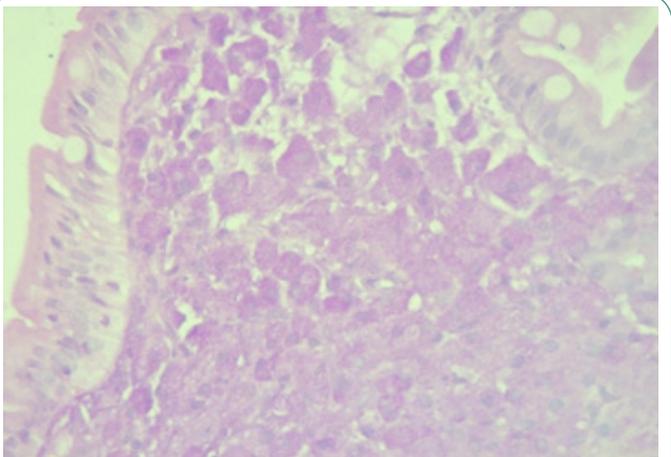
The treatment regimen employed in this case—initial intravenous ceftriaxone followed by a prolonged course of oral trimethoprim-sulfamethoxazole—aligns with established protocols that have demonstrated good prognoses and reduced relapse rates [7,11,12]. The patient's response to treatment was prompt, with significant improvement observed within two weeks and complete resolution of symptoms thereafter. This outcome is consistent with previous literature supporting the efficacy of prolonged antibiotic therapy in achieving remission and preventing recurrence. Long-term follow-up will be mandatory to ensure sustained remission.

### Conclusion

Whipple's Disease (WD) presents a real diagnostic challenge due to its rarity and diverse symptomatology. This case underscores the critical need for clinicians to maintain a heightened suspicion of WD in patients presenting with chronic gastrointestinal symptoms even in the absence of the complete classic symptom triad.



**Figure 1:** H.E. x200 and H.E. x400: Distended villi, expanded by a diffuse foamy macrophage infiltrate, associated to a discrete overlying enterocyte vacuolization.



**Figure 2:** PAS x400: Positive PAS stain of intracytoplasmic bacteria.

In this instance, prompt diagnosis was facilitated through histopathological examination. This highlights the necessity for early recognition and initiation of treatment, crucial for preventing potentially fatal outcomes associated with untreated WD.

Continued vigilance and adherence to treatment protocols are imperative to mitigate the risk of relapse and ensure sustained patient well-being.

Clinicians should be aware of the diverse presentations of WD and not rely solely on the classic symptom triad for diagnosis. A thorough diagnostic evaluation and a high index of suspicion are essential for early detection and effective management. Continued vigilance and adherence to treatment protocols are key to optimizing patient outcomes and preventing the potentially severe consequences of untreated WD. This case serves to reinforce the need for a broad clinical perspective and meticulous diagnostic approach in managing this complex disease.

### Declarations

**Author's contributions:** W Dahmani, I Lassoued: Conceptualization and Writing; N. Elleuch, A Hammami: Formal analysis; S. Mestiri and S. Hmissa: Formal analysis pathological findings; A Ben Slama, A Brahem: Supervision; H Jaziri and M Ksiai: Validation.

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