

Capsule Endoscopy in the Diagnosis, Disease Mapping, and Monitoring of Treatment Response in Gastrointestinal Whipple's Disease

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ABSTRACT

Whipple's disease is a rare systemic infection causing malabsorption. Affected patients often undergo extensive investigation until final diagnosis with periodic acid-Schiff-positive histology. We present the case of a 73-year-old man diagnosed with Whipple's disease after a prolonged history, with a focus on capsule endoscopy (CE) in both mapping the extent of the pathology and follow-up. We demonstrate pre-treatment and post-treatment CE images, allowing visualization of resolved small bowel pathology, and demonstrate histological resolution. The early use of CE in the investigation of Whipple's disease may expedite diagnosis in patients with more distal bowel pathology and help assess disease severity.

INTRODUCTION

Whipple's disease is a systemic bacterial infection caused by *Tropheryma whipplei*, first described in 1907.¹ The disease is rare, with an estimated prevalence of 9.8 per million people in the United States.² Whipple's disease classically involves the gastrointestinal tract, leading to malabsorption; however, any organ may be affected, including the heart and brain.³ Characteristic endoscopy findings include diffuse, distorted, clubbed villi with bowel wall edema.⁴ Although patients may present with significant malnutrition and malaise, they have successfully been treated with long antibiotic courses since 1952.⁵ Relapse is reported in up to 35% of patients.⁶

The presentation of Whipple's disease may be heterogeneous, often leading to delayed diagnosis. We present a case of gastrointestinal Whipple's disease and discuss the utility of capsule endoscopy (CE) in both mapping the extent of disease and proving the effectiveness of antibiotic therapy.

CASE REPORT

A 73-year-old White man was admitted to the hospital with a 2-year history of diarrhea, abdominal pain, weight loss, and leg swelling. He weighed 43 kg on admission; the body mass index was 15.6 kg/m². He reported previous bilateral knee pain with recurrent swelling. His medical history consisted of hypertension, depression, and carotid sinus hypersensitivity. He was an ex-smoker and non-drinker. He worked in school catering. On examination, the patient seemed cachectic with bilateral Dupuytren's contractures. Abdominal examination was unremarkable.

Initial investigations revealed a normocytic anemia (hemoglobin 84 g/L [130–170 g/L], mean cell volume 80.9 fL [80–100 fL]) with iron (5 µmol/L [6–35 µmol/L]) and folate (2.5 µg/L [3.9–20.0 µg/L]) deficiencies. C-reactive protein was raised (64.5 mg/L [0.0–3.0 mg/L]) with hypoalbuminemia (29 g/L [33–55 g/L]). Lactate dehydrogenase, autoimmune screen, and tumor markers were within normal range. Stool tests for routine culture, *Clostridium difficile*, and fecal calprotectin were negative.

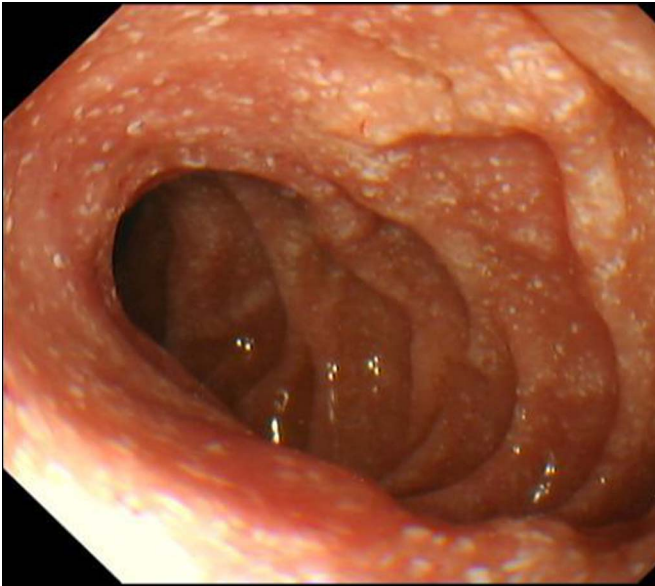


Figure 1. Gastroscopy image demonstrating prominent lymphangiectasia in the proximal jejunum.

An oesophagogastroduodenoscopy (OGD) in 2018, with biopsies obtained from the second part of the duodenum (D2), showed mild duodenitis. Further gastroscopy 1 year later was macroscopically normal.

Computed tomography of the chest, abdomen, and pelvis with contrast was unremarkable. Computed tomography, colonography, and optical colonoscopy revealed uncomplicated diverticulosis only.

A repeat OGD to the jejunum was undertaken with a pediatric colonoscope to exclude small bowel Crohn's disease. This revealed prominent lymphangiectasia between D2 and proximal jejunum (Figure 1).

Jejunal biopsies showed moderate active chronic inflammation with expansion of the lamina propria comprising an associated dispersed population of periodic acid-Schiff stain (PAS)-positive, diastase-resistant foamy macrophages immunoreactive for CD68. These samples were positive for *T. whipplei* DNA on polymerase chain reaction analysis.

Capsule endoscopy was undertaken to map the mucosal extent of lymphangiectasia. An initial patency capsule ensured integrity of the bowel lumen. CE confirmed widespread intestinal lymphangiectasia with villous atrophy, clubbed villi, and erythematous mucosa throughout the jejunum and ileum (Figure 2). Nodular mucosa was observed at a few sites with significant small bowel oedema. There was associated luminal narrowing in the ileum, not seen on OGD. These diffuse findings, coupled with nodularity, were highly compatible with severe small bowel Whipple's disease with associated enteropathy and malnutrition^{4,7}.

The patient commenced intravenous ceftriaxone for 2 weeks and then oral co-trimoxazole 960 mg twice daily for 1 year. His

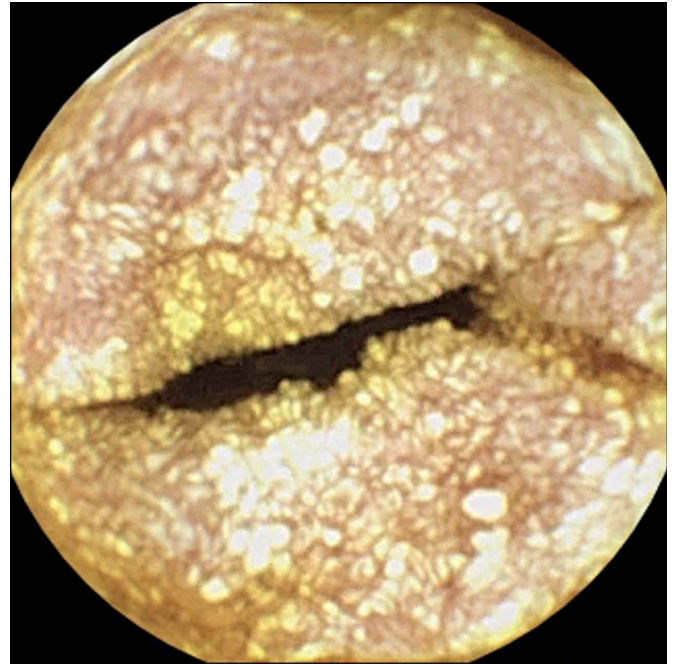


Figure 2. Image of the ileum obtained by MiroView capsule endoscopy demonstrating villous atrophy, lymphangiectasia, and clubbed villi with associated luminal narrowing and nodularity.

symptoms resolved, and his blood tests normalized. His weight increased by 14 kg (body mass index 20.6 kg/m²).

Capsule endoscopy was repeated after antibiotic treatment was complete. The first and second parts of the duodenum appeared normal, with no evidence of lymphangiectasia, nor nodularity as previously described (Figure 3).

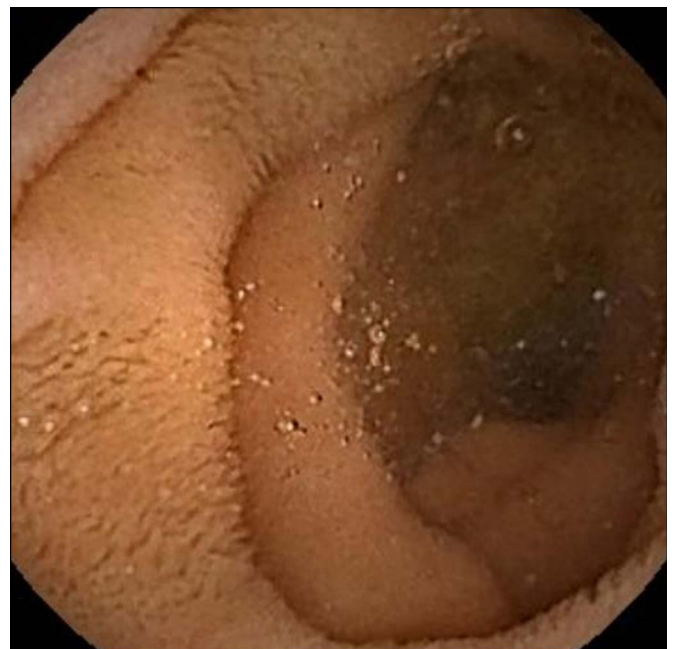


Figure 3. Capsule endoscopy image of the ileum obtained by Pill-Cam shows complete resolution of original pathology after 12 months of antibiotic therapy.

Repeat OGD showed no evidence of duodenitis, and jejunal biopsies showed minimal scattered foamy histiocytes and PAS-positive diastase-resistant granules. This was evidence of near-complete histological resolution. A second polymerase chain reaction test was negative for *T. whipplei* DNA.

DISCUSSION

This case report highlights the utility of CE in diagnosing Whipple's disease, mapping the disease extent and demonstrating resolution of small bowel pathology after antibiotic treatment. Classical Whipple's disease is characterized by abdominal pain, diarrhea, weight loss, and arthralgia. The nonspecific presentation of Whipple's disease may result in a prolonged, unresolved illness. This is emphasized here: A final diagnosis was only reached several years after the patient's initial symptoms.

Gastroscopy with PAS-positive biopsies of the small bowel is diagnostic of Whipple's disease. However, diagnosis using this method is not always possible if more distal segments of the small bowel are affected.

CE is a less invasive method to visualize the entire small intestine and has previously been used to aid in the diagnosis of Whipple's disease where endoscopy was insufficient or poorly tolerated.^{8,9} Few reports describe such findings, and the small bowel phenotype is variable between studies, highlighting the importance of publishing these findings.

In this case, we use CE to fully assess the extent of the disease process. Indeed, there was significant pathology in the ileum which was not visualized on gastroscopy. We also use CE to show complete resolution of the intestinal lymphangiectasia and villous atrophy initially seen using a 1-year course of antibiotics, returning the bowel mucosa toward normality. This correlated with improvement in the patient's symptoms.

Near-complete histological resolution of Whipple's disease was observed. PAS-positive macrophages were visualized on the later duodenal biopsies, although the number of these cells was significantly reduced. The persistence of PAS-positive macrophages may underpin the high rates of relapse in Whipple's disease, highlighting the importance of follow-up in these patients. We plan to review the patient twice a year.

On retrospective analysis, the duodenal biopsies obtained in 2018 stained weakly positive for PAS-positive macrophages. A history of weight loss and symptoms of malabsorption should prompt the pathologist to consider Whipple's disease. We recommend that PAS staining is conducted more regularly in cases of active duodenitis with a clinical presentation suspicious for Whipple's disease.

We suggest that an early use of CE in the investigation of weight loss and malabsorption may expedite a diagnosis of Whipple's disease in

patients with more prominent pathology in the distal small bowel and helps to assess the disease severity. This is important in a disease where prolonged, unresolved presentations are common. The role of CE in guiding treatment duration and predicting the risk of relapse should be the subject of further study.

DISCLOSURES

Author contributions: E. Davenport wrote the manuscript and reviewed the literature; G. Mitsopoulos reported the initial histology slides and provided images; N. Stafford edited the manuscript; A. Sangwaiya provided images and edited the manuscript; and S. Shariq provided endoscopy images, approved the final manuscript, and is the article guarantor.

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