

# Whipple's Disease in an Afro-Caribbean National

DO Whittle<sup>1</sup>, NP Williams<sup>2</sup>, AM Nicholson<sup>3</sup>, K King-Robinson<sup>1</sup>, R Kirsch<sup>4</sup>, R Riddell<sup>4</sup>, T Mazzulli<sup>5</sup>, MG Lee<sup>1</sup>

## ABSTRACT

*Whipple's disease is a rare multi-organ infectious disease caused by Tropheryma whipplei. It is fatal without treatment. We report on a 40-year old Afro-Jamaican man who presented with a six-month history of weight loss and diarrhoea. Investigations revealed iron deficiency anaemia and hypoalbuminaemia. Upper gastrointestinal endoscopy revealed white patchy lesions in the duodenum. The duodenal biopsy showed broadening and thickening of the villi by a dense infiltrate of foamy histiocytes within the lamina propria and focally extending into the attached submucosa. Periodic Acid-Schiff stains were positive. Electron microscopy was confirmatory and polymerase chain reaction testing conclusively identified the organisms as T whipplei. Antibiotic treatment resulted in resolution of symptoms. Although the diagnosis of Whipple's disease is difficult, increased awareness should lead to an increase in reported cases with the improvements in diagnostic capabilities.*

**Keywords:** Antibiotic, diarrhoea, *Tropheryma whipplei*, Whipple's disease

## Enfermedad de Whipple en un Nacional afrocaribeño

DO Whittle<sup>1</sup>, NP Williams<sup>2</sup>, AM Nicholson<sup>3</sup>, K King-Robinson<sup>1</sup>, R Kirsch<sup>4</sup>, R Riddell<sup>4</sup>, T Mazzulli<sup>5</sup>, MG Lee<sup>1</sup>

## RESUMEN

*La enfermedad de Whipple es una rara enfermedad infecciosa multiorgánica causada por el Tropheryma whipplei. Es fatal sin tratamiento. Reportamos un hombre afro-jamaicano de 40 años que se presentó con una historia de seis meses de pérdida de peso y diarrea. Las investigaciones revelaron hipoalbuminemia y anemia ferropénica. La endoscopia gastrointestinal superior reveló lesiones blancas irregulares en el duodeno. La biopsia duodenal mostró la ampliación y engrosamiento de las vellosidades por un denso infiltrado de histiocitos espumosos dentro de la lámina propia, que se extienden hasta la submucosa adjunta. Las tinciones con ácido peryódico de Schiff fueron positivas. La microscopia electrónica fue confirmatoria y la prueba de la reacción en cadena de la polimerasa, identificó los organismos como T whipplei de forma concluyente. El tratamiento antibiótico trajo como resultado la resolución de los síntomas. Si bien el diagnóstico de la enfermedad de Whipple es difícil, un aumento de la conciencia debe conducir a un aumento en los reportes de casos divulgados que reflejan un mejoramiento en la capacidad para hacer el diagnóstico.*

**Palabras claves:** Antibiótico, *Tropheryma whipplei*, diarrea, enfermedad de Whipple

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## INTRODUCTION

Whipple's disease is a rare multi-organ infectious disease caused by *Tropheryma whipplei* (*T whipplei*), and it is gener-

ally accepted that both the presence of the bacillus and the host response are responsible for its clinical manifestations (1–5).

The incidence of this disease is rare with cases occurring predominantly in white males (6–7). The clinical manifestations can be quite variable but gastrointestinal symptoms are usually the first to appear in most patients (8). The disorder has not been reported previously from the English-speaking Caribbean countries. We present a case of Whipple's disease in an Afro-Caribbean patient from Jamaica.

From: <sup>1</sup>Department of Medicine, <sup>2</sup>Department of Pathology and <sup>3</sup>Department of Microbiology, The University of the West Indies, Kingston 7, Jamaica, <sup>4</sup>Department of Pathology and Laboratory Medicine and Microbiology, Mount Sinai Hospital, Toronto, Canada and <sup>5</sup>University of Toronto, Toronto, Canada.

Correspondence: Professor MG Lee, Department of Medicine, The University of the West Indies, Kingston 7, Jamaica.  
E-mail: michael.lee@uwimona.edu.jm

## CASE REPORT

A 40-year old man presented with a six-month history of weight loss and diarrhoea. He was known to have mental retardation since birth. He did not attend school and was taken care of by relatives. He was able to carry out activities of daily living, and hold simple conversations. He had no other known illnesses.

He was relatively well until six months previously, when he developed diarrhoea and started losing weight. He reported approximately four daily episodes of brown, watery, small volume stools in association with vague generalized abdominal pain and anorexia. He later noticed intermittent abdominal distension and discomfort. There was no history of fever or night sweats. The patient was not on any medication and he denied haematochezia, greasy stools, history of recent travel or ill contacts. He sought medical attention and was given antibiotics which resulted in temporary cessation of the diarrhoea. However, the diarrhoea returned approximately one week after completing the course. A few episodes of nausea and vomiting were noted two weeks prior to presentation. Vomitus consisted of previously eaten food, without blood.

His past medical history was significant for longstanding constipation. This resolved spontaneously approximately 20 years ago with the passage of regular brown stool approximately once daily until six months prior to presentation.

Examination revealed a young, small built male with mild general muscle wasting. His vital signs were normal. There was no lymphadenopathy or icterus. His abdomen was soft, globally distended and non-tender with no organomegaly. His neurological examination showed lack of orientation to time and place but he was cooperative. His speech was fluent, slow but comprehensible. His memory was impaired. Cranial nerve examination was normal while motor examination revealed decreased muscle bulk but normal power. Sensory examination was normal.

Investigations revealed iron deficiency anaemia, normal electrolytes and hypoalbuminaemia. HIV and HTLV-1 tests were negative. Colonoscopy with biopsy was normal. Upper gastrointestinal endoscopy revealed white patchy lesions in the duodenum (Fig. 1).

On histology, the duodenal biopsy showed broadening and thickening of the villi by a dense infiltrate of foamy histiocytes within the lamina propria and focally extending into the attached submucosa (Fig. 2). Periodic Acid-Schiff (PAS) stains were positive (Fig. 2) and the diagnosis of Whipple's disease was made. Electron microscopy on the duodenal biopsy was confirmatory and polymerase chain reaction (PCR) testing conclusively identified the organisms as *T. whipplei* (Fig. 3).

A computed tomography (CT) scan of the brain and lumbar puncture were both normal. Echocardiogram revealed no cardiac abnormality. Slit lamp examination of the eyes was unremarkable. His evaluation by the psychologist confirmed severe mental retardation. Intravenous antibiotic therapy was commenced with ceftriaxone (2 g intravenous twice daily) for

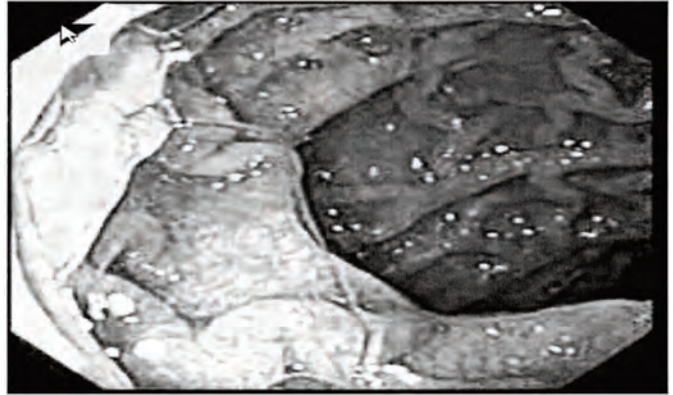


Fig. 1: White patches in the duodenum.

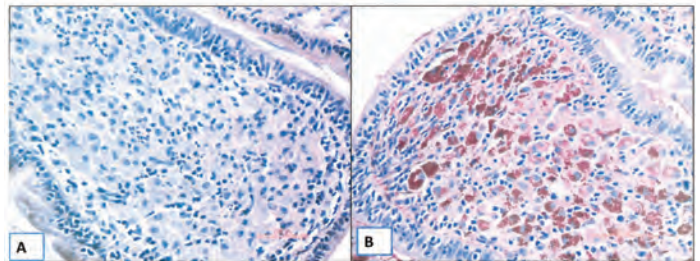


Fig. 2: Duodenal biopsy showing distension of villous by numerous foamy macrophages with interspersed sprinkling of neutrophils (H&E) – A, and bright red Periodic Acid-Schiff positive staining of *T. whipplei* – B.

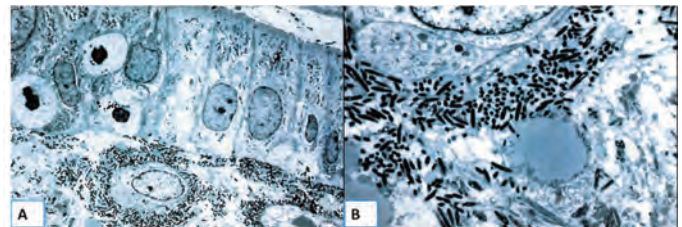


Fig. 3: Electron microscopic image showing numerous electron intracytoplasmic dense rods within subepithelial macrophages – A, and at higher magnification, numerous bacilli consistent with *T. whipplei* – B.

two weeks followed by prolonged (one year) co-trimoxazole orally (Bactrim double strength one tablet twice daily). Upon review several months later, his diarrhoea had resolved and he had gained weight.

## DISCUSSION

Whipple's disease is a rare systemic infectious disorder, first described by George Whipple in 1907 and first diagnosed in life in 1947 (8). It is caused by the organism *Tropheryma whipplei*, a gram positive bacillus. The incidence rate of Whipple's disease is extremely low and thus there is no accurate estimate of either the prevalence or mortality rate (6, 9). The occurrence of classical Whipple's disease in Africans and persons of African descent and in the English-speaking Caribbean is rare and this is the first reported case from this region. It is suggested that genetic factors may determine the clinical

manifestation of *T whipplei* infection and that classical Whipple's disease is just one possible rare manifestation (10).

The diagnosis of Whipple's disease is difficult, with the usual bacterial culture methods failing to grow the organism. Successfully culturing *T whipplei* with a different approach, using human fibroblast cell line (HEL) has been reported (11). The organism was shown to be slow growing with a very long doubling time. This method has not been accepted for routine use and the diagnosis of Whipple's disease is made by demonstrating characteristic lesions in tissue obtained from biopsy of affected organs, such as the duodenum and eyes. It is characterized by accumulation of macrophages in the lamina propria with intensely PAS positive intracellular material (12). Upper gastrointestinal endoscopy with biopsies of the small intestine is the diagnostic test of choice (13). Positive PAS-stained macrophages infiltrating body tissues are, however, not pathognomonic for Whipple's disease. These macrophages can also be detected in infections observed in patients who are immunosuppressed with HIV infection. Diagnostic electron microscopy reveals coccobacillary bodies that represent the *T whipplei* organism, which is diagnostic. Polymerase chain reaction for *T whipplei* nucleic acid will be positive in the affected tissue(s) (14–16).

Asymptomatic carriers of *T whipplei* have been described. Therefore, an isolated positive PCR for *T whipplei* in gastrointestinal mucosa or contents is not sufficient for a definitive diagnosis of Whipple's disease. Nevertheless, where the clinical picture is suggestive of the disease, PAS positive macrophages on histology of appropriate specimens is classically considered diagnostic and a positive PCR is regarded as confirmatory for Whipple's disease (6).

Clinically, Whipple's disease is characterized by two stages: a prodromal stage and a much later steady-state stage. The prodromal stage is characterized by variable findings, mainly arthralgia and arthritis. The steady-state stage is typified by weight loss, diarrhoea, or both. Occasionally, due to involvement of other organs, patients may develop skin and ocular manifestations (uveitis, retinitis, optic neuritis), generalized lymphadenopathy, blood culture-negative endocarditis which may be complicated by cardioembolic strokes, and a sarcoidosis-like syndrome with mediastinal lymph nodes and central nervous system (CNS) involvement.

Gastrointestinal complaints typically precede CNS symptoms by several years. In our case, the patient was born with mental retardation, which is not one of the manifestations described in the literature. Despite concerns that this may have been a manifestation of CNS involvement, his gastrointestinal symptoms resolved with treatment while his mental status remained the same, indicating that it was unlikely to be a part of the disease process.

Whipple's disease is fatal without treatment. Tetracycline had been the mainstay of therapy for many years, before a comprehensive review demonstrated a relapse rate of 35% among patients treated primarily with this agent (17). The rate of CNS relapse was also high, and re-treatment of CNS relapse

with tetracycline was not effective. Subsequent management has consisted of parenteral ceftriaxone followed by oral trimethoprim-sulfamethoxazole (TMP-SMX) maintenance therapy for one year. The rationale for prolonged therapy is to permit complete eradication of the organism, thereby reducing the likelihood of relapse. Treatment with TMP-SMX appears superior to tetracycline in inducing clinical remission (18). In addition, TMP-SMX has been more effective for CNS disease although it is not curative in all cases.

The response to treatment can be monitored by following the patient's haematocrit, weight, and symptom resolution. Surveillance endoscopy and small bowel biopsy are not necessary and may be misleading since PAS positive material may persist long after clinical resolution of the disease. It has been suggested, however, that follow-up PCR testing may have greater predictive value (15).

*T whipplei* appears to be widely present in the environment and postulated to be in soil and water. It has been suggested that host factors indicated by immune deficiencies are responsible for the development of Whipple's disease. Recent data demonstrate a persistent defect of the cellular immune response (19).

It is likely that subclinical or transient cases of Whipple's disease and other manifestations of infection with *T whipplei* will be discovered in the years to come as our knowledge improves regarding the natural history of the disease, given the improvements in diagnostic capabilities.

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