

## **Mycobacterium infection of the duodenum mimicking Whipple's disease**

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*This paper reports a case of 42-year-old male who was found to be infected with the human immunodeficiency virus (HIV). He developed low-grade fever with cough. Evaluation led to a diagnosis of pulmonary tuberculosis. He was then treated with antituberculous drugs. He was also admitted for further investigation, after suffering diarrhea, abdominal pain and upper gastrointestinal bleeding.*

*Esophagogastroduodenoscopy revealed esophagitis, gastritis, and severe duodenitis. Biopsies showed broad, fused villi with foamy macrophages filling the lamina propria. We report the pathologic means to differentiate atypical mycobacterial infection from Whipple's disease which had resembling pathologic picture. This case is unique in that despite clinical and light microscopic features similar to Whipple's disease, the inciting organism is compatible with Mycobacterium avium intracellulare, a frequent opportunistic infection in AIDs patient.*

**Key words** : *Mycobacterium avium-intracellulare infection, Tuberculous duodenitis.*

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นฤมล วิเศษโอกาส, เสาวณีย์ เย็นฤดี. วัณโรคของลำไส้เล็กส่วนต้นในผู้ป่วยโรคเอดส์.  
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รายงานผู้ป่วยเพศชายอายุ 42 ปี มีประวัติเป็นโรคเอดส์ ต่อมามีอาการไข้ต่ำๆ และไอ ตรวจพบว่าเป็นวัณโรคปอด ผู้ป่วยได้รับการรักษาจนครบสมบูรณ์ หลังจากนั้นผู้ป่วยมีอาการผิดปกติของทางเดินอาหาร ตรวจพบมีการอักเสบของหลอดอาหาร กระเพาะอาหาร รวมทั้งพบมีการอักเสบอย่างรุนแรงของลำไส้เล็กดูโอเด้นัม แพทย์ผู้รักษาได้ตัดชิ้นเนื้อจากบริเวณดังกล่าว และส่งตรวจทางพยาธิวิทยา ผลการตรวจทางพยาธิวิทยาพบมีการเปลี่ยนแปลงที่เข้าได้กับพยาธิสภาพของโรคที่เกิดจากเชื้อ *M.avium-intracellulare* ที่พบในผู้ป่วยโรคเอดส์ซึ่งมีพยาธิสภาพที่คล้ายคลึงกับโรค Whipple's ผู้รายงานได้กล่าวถึงวิธีการศึกษาทางพยาธิวิทยาที่สามารถแยกโรคนี้จากโรค Whipple's โดยใช้การย้อมพิเศษเพื่อศึกษาแยกเชื้อที่เป็นสาเหตุของโรคดังกล่าว

The gastrointestinal tract is a major target for opportunistic infections in human immunodeficiency virus (HIV) infection, and gastrointestinal symptoms such as weight loss, diarrhea, and abdominal pain are common among HIV - infected patients.<sup>(1-3)</sup>

This paper reports a case of a patient with acquired immunodeficiency syndrome whose clinical presentation and histologic features resembled Whipple's disease. The unique feature of this case was the absence of Whipple's bacilli and the presence of Mycobacterium within macrophages infiltrating the duodenal lamina propria.

### Case Report

A 42-year-old male who had multiple sexual partners was found to be infected with HIV. He remained asymptomatic for three years until developing low-grade fever with cough and pulmonary tuberculosis, in June 1996. Treatment with isoniazid, rifampin, ethambutol, and zidovudine was provided for six months. Over the next four months, the patient's symptoms continued. Persistent watery diarrhea, progressive weight loss and left upper quadrant abdominal pain led to further evaluations in April 1997. Stool examination revealed negative results for leukocytes, ova, parasites, and cryptosporidium. The abdominal ultrasonogram showed enlargement of the parapancreatic lymph nodes and a left lower quadrant mass. Therapy with antituberculous drugs was reinitiated. The patient had no response to those drugs.

The patient was admitted to Chulalongkorn Hospital in June 1997, with diarrhea, abdominal pain, and upper GI bleeding. Examination revealed an emaciated, chronically appearing male with a temperature of 38.5°C. A chain of lymph nodes were palpated in the cervical area. Lungs were clear. Abdominal examination yielded hepatomegaly with mild tenderness at the left upper quadrant. There were no joint abnormalities.

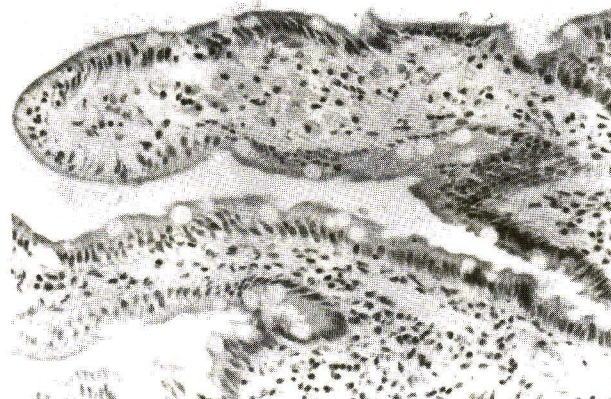
Laboratory data included a hemoglobin count of 7.24 mg/dl; a white blood cell count to 1890 cell/mm<sup>3</sup> (37.7% polymorphonuclear leukocytes, 29% lymphocytes, and 26.6% monocytes); and a platelet count of 394,000 cell/mm<sup>3</sup>. Additional blood tests disclosed serum glutamic oxaloacetic transaminase (SGOT) 51 U/L; alkaline phosphatase 537 U/L; and albumin 3.6 g/dl. Blood and stool cultures were negative. Stool examination demonstrated no white blood cells, ova, or parasites. Sputum stains were negative for acid fast bacilli.

The patient underwent esophagogastroduodenoscopy which showed esophagitis with a white exudate, mild gastritis, and severe duodenitis with a whitish exudate covering its mucosa. Biopsies of the esophagus and duodenum were done. Fresh KOH preparation revealed negative fungal infection.

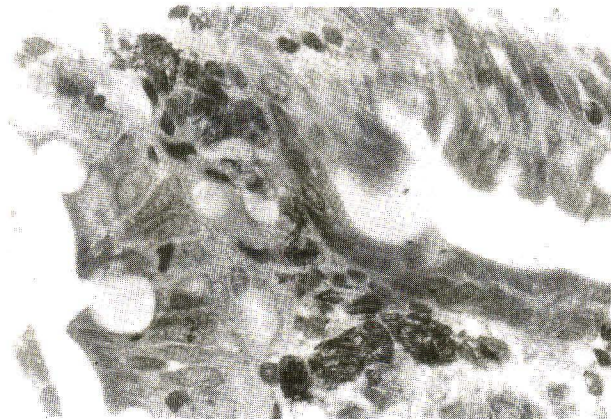
Histological examination of tissue from the duodenum exhibited mixed mononuclear cell infiltration of the lamina propria. Foam cell infiltration with some short and widening villi were present (Figure 1). The esophageal mucosa

displayed hyperplasia and focal mononuclear cell infiltration in the submucosa. Some PMN were seen dispersingly in the mucosal epithelium. Acid-fast stains in the exhibited bacilli within these macrophages and free in the lamina propria (Figure

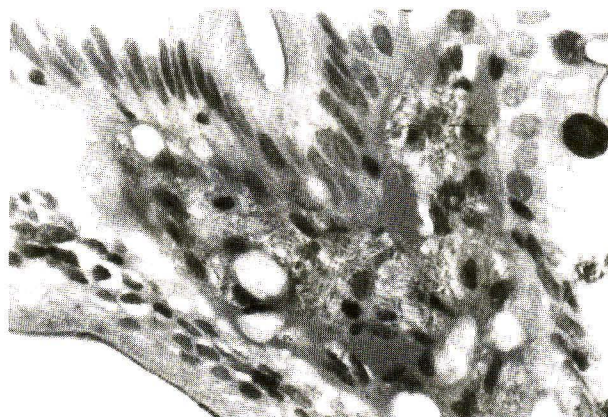
2). These macrophages also exhibited PAS-positive diastase-resistant rodlike material (Figure 3). This appearance was felt to be consistent with mycobacterial species. After discharge, the patient received treatment for disseminated tuberculosis.



**Figure 1.** Endoscopic duodenal biopsy of broad villi filled with "foamy" macrophages infiltration the lamina propria (H & E, x 100).



**Figure 2.** Large numbers of acid-fast bacilli packing in the cytoplasm of macrophages (Ziehl-Neelsen, x 400).



**Figure 3.** Paraffin-embedded section of duodenum stained by PAS method showing numerous PAS-positive bacilli seen in macrophages (x 400).

## Discussion

The clinical presentation of this case suggested diagnosis should be a Whipple's disease because of a morphologic picture which was subsequently found to reflect *Mycobacterium avium* infection. Whipple's disease is an uncommon intestinal disorder, characterized by diarrhea, abdominal pain, anorexia, weight loss, migratory arthritis, and steatorrhea. Characteristic pathologic findings include villus widening, foamy macrophages in the lamina propria filled with periodic acid-Schiff (PAS) staining material, and dilated lymphatics. While no specific organism has been cultured, treatment with tetracycline or other broad spectrum antibiotics is usually curative.<sup>(4)</sup>

It has become clear that the gastrointestinal (GI) tract is a major target organ in AIDS patients. Speculation about etiologic causes has included malnutrition, deficiencies of trace minerals, viruses, and other presumed, but unidentified, infections. With regard to the infectious causes of diarrhea, AIDS patients can have the traditional infections of the immunocompetent host, as well as those infections unique to the immunoincompetent. In this latter group, infection with *Mycobacterium avium-intracellare* (MAIC) has been identified.

MAIC, known to be a common commensal organisms in the environment was previously a rare pathogen with only 50 cases of human infection reported prior to 1982.<sup>(5)</sup> With the AIDS epidemic, however, disseminated MAIC infection has been recognized frequently.<sup>(6)</sup> In 1982, gut involvement was first reported; it was discovered on postmortem

examination.<sup>(7)</sup> A year later, a duodenal lesion microscopically resembling Whipple's disease was reported to be due to MAIC infection.<sup>(8)</sup> Duodenal involvement was most common and was occasionally accompanied by a characteristic gross lesion, that of fine white nodules on the mucosa.<sup>(9)</sup> Autopsies which identified MAIC infection in tissue, emphasized the heavy burden of organisms in histiocytes, the absence of formed granulomas, and the extensive tissue invasion.<sup>(10-12)</sup> In addition, the organisms are highly resistant to conventional antimycobacterial agents.<sup>(13)</sup>

Because of the difference in therapeutic approach, it is important to distinguish Whipple's disease from MAIC infection when the histologic picture of PAS-positive bacilli within intestinal macrophages is observed.

Even without culture data or electron-microscopic examination, acid fast stains of tissue can be used to differentiate between the two conditions. Microorganisms in Whipple's do not stain with acid-fast tissue stains. The Ziehl-Neelsen stain reacted with the bacterial inclusions in macrophages in our case. When PAS-positive macrophages are seen within intestinal biopsies, a diagnosis of Whipple's disease should no longer be made until acid-fast stains have been carried out.

Because of a large number of MAIC infections observed thus far in patients with AIDS, MAIC should be suspected when a histologic picture similar to Whipple's is seen in this group of patients, even if no cultures had yet been reported.

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