CASE REPORT

Whipple's Disease

Characterization of Anaerobic Corynebacteria and Demonstration of Bacilli in Vascular Endothelium

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The first patient with a well documented case of Whipple's disease, in whom an anaerobic Corynebacteria was successfully cultured both from the mucosa of the small intestine and from mesenteric lymph nodes is described. Electron microscopic studies demonstrated the organisms in the mucosa of the small intestine and in lymph nodes. In addition, vascular invasion was observed and the vascular endothelium contained a large number of bacilli. These observations support the concept that anaerobic Corynebacteria may be important in Whipple's disease, but the precise role of this organism in the pathogenesis of this disorder remains to be elucidated.

Whipple's disease is a rare disorder characterized clinically by the presence of arthralgias, abdominal pain, fever, diarrhea, progressive weight loss and malabsorption syndrome (1). Laboratory studies usually reveal the presence of anemia, hypoalbuminemia, abnormal small bowel roentgenograms, impaired xylose absorption and steatorrhea. In Whipple's original report, bacilli were isolated from mesenteric lymph nodes. However, relatively little attention was directed towards the concept of an infectious etiology in Whipple's disease until 1961, when Yardley and Hendrix described "bacillary bodies" in the lamina propria of the small intestine and suggested that these bodies were bacteria (2). In the past decade, there have been several reports demonstrating the presence of bacilliform bodies in the small intestine (3-5), lymph nodes (5-7), and most recently, the brain (8) of patients with Whipple's disease. Despite the fact that the presence of bacilliform bodies is usually associated with active disease, the exact role of the bacilli in the pathogenesis of the disease is unclear. This is due, in part, to the frequent failure to culture microorganisms from the small intestine of patients with Whipple's disease (9, 10). In this regard, there have been only 5 reports (11-15) which have implicated Corynebacteria microorganisms.

The present report describes a patient with well-documented Whipple's disease in whom a Corynebacterium anaerobium was cultured from both the mucosa of the small intestine and from mesenteric lymph nodes. Electron microscopic studies demonstrated the organisms in the mucosa, lymph nodes, and also in endothelial cells lining the blood vessels.

CASE REPORT

A 41 year-old farmer was admitted to the Ohio State University Hospital because of progressive...
weight loss. During the 4 months before hospitalization, the patient experienced a 17-pound weight loss, anorexia and fatigue. Low-grade fever, abdominal distention, borborygmi and a dull epigastric pain had also been noted. In addition, the patient complained of having 4–5 loose stools per day but without melena or hematochezia. There was no history of arthralgias and the patient had not traveled outside the USA.

On admission to the University Hospital, physical examination revealed an emaciated, somewhat irascible, white man. His temperature was 98°F, pulse 96, respirations 16 and his blood pressure was 110/70 mm Hg. There was no lymphadenopathy. Examination of the heart and lungs was normal; the abdomen was distended and tympanitic; the liver and spleen were not palpable, but there was shifting dullness suggesting the presence of ascitic fluid. Neurologic examination was unremarkable except for the presence of mild confusion and disorientation.

Laboratory examination revealed a hemoglobin of 7.3 g/100 ml and hematocrit 23%. Peripheral blood smear showed normochromic and normocytic red cells; the white blood cell count was normal. Serum folate was 4.3 mg/100 ml (normal 7–16) and serum vitamin B₁₂ was 18.8 μg/100 ml (normal 200–650). Bone marrow aspiration showed maturation arrest, plasmacytosis and changes in myeloid elements consistent with folic acid deficiency. Blood urea nitrogen (BUN), serum creatinine, sodium, potassium, chloride, CO₂ combining power, fasting blood sugar, uric acid, bilirubin, lactate dehydrogenase (LDH), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase, calcium and phosphorus values were all within normal limits. Prothrombin time was 100%. Serum protein electrophoresis revealed an albumin value of 2.6 g/100 ml and globulins of 2.8 g/100 ml. Stool examination for ova and parasites, on 3 occasions, was negative. Qualitative stool-fat examination showed a normal amount of neutral fat but increased amounts (3+) of split fats. There were no undigested muscle fibers. The quantitative stool-fat collection was inadvertently discarded. X-ray studies of the small intestine revealed dilatation of the entire small bowel, coarsening of the mucosal folds and segmentation of the barium column.

An oral small bowel biopsy was obtained from the proximal jejunum and revealed changes characteristic of Whipple’s disease. In an attempt to define, more clearly, the bacteriologic abnormalities in this disease, we chose to perform an exploratory laparotomy. The patient was fully informed of the risks and reasons for this procedure, for which he gave his consent. At laparotomy, the abdomen contained approximately 700 ml of ascitic fluid. In addition to samples of ascitic fluid and portal blood, two mesenteric lymph nodes and a specimen of jejunum were obtained for further study (see below). The patient made an uneventful recovery from laparotomy and after 7 days was started on tetracycline 250 mg, 4 times daily. Thereafter, he improved rapidly; his symptoms of anorexia, fatigue, fever and diarrhea abated and during the next 3 months, he gained 30 pounds. Followup examination, after 6 months of tetracycline therapy, revealed a normal hematocrit (41%), hemoglobin (14 g/100 ml), routine serum chemistries, fecal fat excretion (5 g/24 hr), and urinary excretion of D-xylose (5.3 g/5 hr).

**MATERIALS AND METHODS**

All specimens of tissue used for bacteriologic and electron microscopic studies were obtained at the time of exploratory abdominal laparotomy. No previous treatment with antibiotics had been given. Twenty milliliters of “portal” blood were obtained under sterile conditions from a jejunal mesenteric vein along with 100 ml of ascitic fluid, and immediately sent for detailed bacteriologic studies. Two mesenteric lymph nodes and a single full-thickness biopsy of the mid-jejunum were obtained for culture and light and electron microscopic studies.

**Bacteriology.** The jejunal tissue was washed 15 times with normal saline. Specimens of jejunum, mesenteric lymph node and portal blood were cultured on thioglycollate broth, chocolate broth, trypticase soya broth and trypticase soya broth enriched with 1% yeast extract. All growth on these cultures was subcultured aerobically and anaerobically on chocolate agar plates, trypticase soya broth and trypticase soya broth enriched with 1% yeast extract. All growth on these cultures was subcultured aerobically and anaerobically on chocolate agar plates, trypticase soya plates and trypticase soya plates with 1% yeast extract.

**Light microscopy.** Specimens were immediately fixed in 15% formalin at a pH of 7.8–8.0, processed in an Auto-Technicon Model 2A, and embedded in paraffin base blocks. Using an “820” Spencer microtome, 4-μm thick sections were cut and stained with standard hematoxylin and eosin, periodic acid-Schiff (PAS) and Gram stains.

**Electron microscopy.** Lymph node and intestinal biopsies were fixed in 3% glutaraldehyde for 2