Treponema pallidum and Helicobacter pylori
Recovered in a Case of Chronic Active Gastritis

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A 49-year-old man complaining of epigastric pain underwent endoscopy, during which thickened stomach folds below the fundus were observed. Microscopic examination of gastric tissue biopsy specimens revealed chronic active gastritis. Dieterle stain revealed overwhelming numbers of "corkscrew-like" spirochetes. These were proved to be consistent with Treponema pallidum.

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A comprehensive study of the tissue revealed the added presence of Helicobacter pylori. This appears to be the first case report describing the involvement of H. pylori and T. pallidum together in a case of chronic active gastritis. (Key words: Treponema pallidum; Helicobacter pylori; Chronic active gastritis; Syphilitic gastritis) Am J Clin Pathol 1992;97:116-120

Helicobacter pylori, a spiral microorganism commonly recovered from antral and peptic ulcer disease, is a recent addition to the list of potential human pathogens. The precise role for this microorganism in the process of gastric ulceration is not known.1 Treponema pallidum, the etiologic agent of syphilis, is always correlated with disease. These microorganisms were recovered in a recent case of chronic active gastritis. Syphilitic gastritis is a rare clinical disease. From 1960 to 1985, few reports of gastric syphilis were published,2-9 presumably because of the disappearance of syphilis. However, the incidence of untreated primary syphilis has increased since 198510 and new cases of gastric syphilis11-14 have been reported. We report a case of gastric syphilis in which H. pylori and T. pallidum were recovered.

CASE REPORT

A 49-year-old man was evaluated for complaints involving the abdomen. He was anorexic, experienced chronic nausea lasting 1 month, and lost 20 pounds in a period of several months. He experienced early satiety followed by emesis after meals. There was no change in his bowel habits. A macular rash was observed over his trunk, arms, legs, palms,
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and soles. Results of serologic tests for syphilis were positive, including the serum rapid plasma reagin, Venereal Disease Research Laboratory (VDRL) (titer 1:64), fluorescent treponemal antibody absorption (FTA-ABS), and cerebrospinal fluid VDRL. No central nervous system defects were noted. A human immunodeficiency virus test result was negative. An upper gastrointestinal endoscopy was performed and the esophagus and fundus of the stomach appeared normal. The corpus of the stomach consisted of thickened folds with friable mucosa. Multiple serpiginous ulcers with exudate were observed. Biopsy and brushing specimens were obtained. Spirochetes were observed with the Dieterle stain. The patient was admitted to the hospital for therapy. Partially healed chancres were noted on the ventral and dorsal penile surfaces. Four million units of penicillin was administered intravenously every 4 hours for 10 days. The Jarisch-Herxheimer reaction was not observed and penicillin therapy was tolerated very well. The rash remained on the body torso through 8 days of therapy. After therapy, his symptoms resolved, he gained weight, and was discharged to his home. The patient was reexamined after 1 month and at 3 months but follow-up endoscopic examinations were not performed.

MATERIALS AND METHODS

Histologic Procedures

Formalin-fixed, paraffin-embedded gastric tissue sections were stained with hematoxylin and eosin, Brown and Brenn Gram's stain, and Dieterle silver stain. A direct immunofluorescence antibody test using monoclonal and polyclonal anti-Treponema pallidum antibody was performed on a section of gastric tissue at the Centers for Disease Control, Atlanta, Georgia.

Serologic Procedures

Immune status tests included syphilis by the rapid plasma reagin (Becton Dickinson, Cockeysville, MD), VDRL, and FTA-ABS (both performed at Connecticut State Department of Health, Hartford, CT); human immunodeficiency virus enzyme immunoassay (Ortho Diagnostics, Raritan, NJ); anti-H. pylori antibody (SmithKline Beecham Clinical Laboratories, Waltham, MA); and Borrelia burgdorferi immunoglobulin (Ig) G and M enzyme immunoassays (North American Laboratory Group [NALG], New Britain, CT).

Immunocytochemical Procedures

Rehydrated gastric tissue sections were incubated overnight with a 1:200,000 dilution of monoclonal anti-Campylobacter spp. antibody (Bioproducts for Science, Inc., Indianapolis, IN). This antibody was shown previously to label H. pylori. Visualization of the primary antibody binding to the target antigen was achieved by sequential application of biotinylated F(ab)2 fragmented rabbit antimouse IgG (DAKO Corporation, Carpinteria, CA), peroxidase conjugated streptavidin (Jackson ImmunoResearch Laboratories, Inc., West Grove, PA), and 3-amino-9-ethylcarbazole (Sigma Chemical Co., St. Louis, MO).

Serum Electrophoresis

A Western blot to detect antibodies to B. burgdorferi and T. pallidum (treponemal antigens courtesy of Victoria Wicher, Albany Medical College, Albany, NY) was performed as described previously (NALG, New Britain, CT) on serum drawn from the patient at each examination.

In Situ Polymerase Chain Reaction

The polymerase chain reaction was performed as described previously to detect DNA sequences for B. burgdorferi.

RESULTS

Radiologic and Endoscopic Findings

A poorly distensible antrum with thickening was observed, which was consistent with linitis plastica. The esophagus and fundus appeared normal. The corpus and the antrum exhibited grossly thickened folds, friable mucosa, and serpiginous ulcers throughout (Fig. 1).

FIG. 1. The photomicrograph taken during endoscopy is in the area of the antrum and reveals edematous folds with hemorrhage and superficial ulceration.
**Gastric Biopsy**

The hematoxylin and eosin stain of several tan to red mucosal fragments showed an active chronic inflammatory response in the lamina propria consisting of increased numbers of mononuclear cells and neutrophils. Plasma cells were present, but not in unusual numbers. Polymorphonuclear leukocytes were observed lining the epithelium of the gastric glands, which showed inflammatory reactive cytologic changes. The gastric glands were reactive. Exudate was present and consisted of mononuclear cells, polymorphonuclear leukocytes, and lymphoid cells. Foci of fibrinous material containing karyorrhectic debris was consistent with an ulcerous bed. A Dieterle stain revealed the presence of spirochetes that were morphologically consistent with *Treponema spp.* (Fig. 2). The direct immunofluorescence antibody test for the presence of *T. pallidum* in a section of the gastric tissue was interpreted as "...reactive: *Treponemes* morphologically resembling pathogenic *Treponema* were observed by direct immunofluorescence" (results from the Treponemal Research Laboratory, Centers for Disease Control, Atlanta, GA, January 1991).

**Serologic Findings**

The rapid plasma reagin, VDRL, and FTA-ABS tests were positive for sera drawn at the initial examination, at 1 month, and at 3 months after treatment. The VDRL decreased in titer from 1:64 to 1:4 during that 3-month interval. The human immunodeficiency virus antibody test was negative. Antibodies to *H. pylori* were positive for IgG and IgA. The IgG titer to *B. burgdorferi* was 1:2560 and the IgM was negative.

**Immunocytochemical Findings**

*Helicobacter pylori* was identified in formalin-fixed gastric tissue biopsy sections with immunoperoxidase labeling. A careful reexamination of the gastric tissue sections revealed *H. pylori* in distinct gastric crypts stained by the Dieterle and Brown and Brenn Gram stains (Fig. 3).

**Serum Electrophoresis**

The patient's serum revealed band identity with a known anti-*T. pallidum* human sera control when tested against treponemal antigens. Cross-reacting bands to *B. burgdorferi* antigens were noted between the marker area of 47,000 to 96,000 daltons.

**In Situ Polymerase Chain Reaction**

Studies of the gastric biopsy specimens for amplification of *B. burgdorferi* genetic sequences were negative.

**DISCUSSION**

The association of *H. pylori* with active chronic gastritis has become well accepted within the last few years. The microorganism has been observed by histologic and microbiologic methods from ulcerous lesions located in the antrum of the stomach, and...
in the duodenum. However, because recovery of the microorganism from asymptomatic populations is increasingly prevalent with advancing age, a case for a precise role defining gastritis with the microorganism cannot be made. *Helicobacter pylori* has been called a quiescent pathogen of the gastrointestinal tract.

Published reports of the gastric involvement of *T. pallidum* have waned during the last 30 years. Recent reports have made no attempt to exclude other spiral bacteria in their specimens, including *H. pylori*, *Borrelia spp.*, or unidentified spiraliform bacteria. A recent speculation postulates that achlorhydria due to pernicious anemia may be caused by the presence of *H. pylori*. Interestingly, a case of antral gastric syphilis with associated pernicious anemia was reported.

The positive enzyme immunoassay titer to *B. burgdorferi* was proved to be a strong cross-reaction to the *T. pallidum* on the basis of the few reacting bands on the Western blot and a negative polymerase chain reaction. There are no reports addressing the potential antigenic cross-reaction of *T. pallidum* and *H. pylori* in the immunoperoxidase stain.

Some investigators have reported problems with silver staining in the process of visualizing spirochetes; some prefer the Warthin-Starry stain, or the Dieterle stain, or immunofluorescence and immunoperoxidase staining. The numbers of *T. pallidum* were overwhelming in our sections, making treponemal detection easy. Conversely, we used immunoperoxidase to detect *H. pylori* because making morphologic distinctions between spirochetes and spirofilars became impossible.

The high-dose intravenous penicillin therapy was aimed at the central nervous system eradication of *T. pallidum*. It probably eradicated *H. pylori* concurrently. Oral therapy for *H. pylori* involves the use of bismuth and a systemic anti-microbial agent. *H. pylori* is susceptible to penicillin treatment. Because a post-treatment antral biopsy was not obtained, we cannot be assured of recrudescence of *H. pylori* in the patient’s antrum.

**REFERENCES**


