

Symptomatic Gastric Sarcoidosis and *Helicobacter pylori* Infection

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Sarcoidosis is a multiorgan granulomatous disease of undetermined cause most commonly affecting young adults and typically characterized by pulmonary infiltrates, bilateral hilar lymphadenopathy, and cutaneous and ocular lesions.¹ Gastric involvement is the second most common site of gastrointestinal involvement after the liver, although the overall incidence of gastric sarcoidosis is still unclear. Palmer² found sarcoid granulomas in the biopsy specimens of 6 of 54 patients who had sarcoidosis but no gastrointestinal symptoms, suggesting an incidence of up to 10 percent; however, biopsy sampling error could have resulted in underestimating the actual frequency of the disease.³ Nevertheless, the frequency of symptomatic gastric sarcoidosis based upon case reports might be as little as 1 percent.⁴

Gastric sarcoidosis results in symptoms similar to those of peptic ulcer disease,⁵ upper gastrointestinal hemorrhage,⁶⁻⁹ or gastric outlet obstruction.¹⁰ There are reports of gastric sarcoidosis being mistaken for infiltrating gastric carcinoma because of their similar clinical manifestations and the linitis plastica radiographic appearance common to both.^{11,12} The relation between the granulomatous mucosal changes seen in gastric sarcoidosis and in peptic ulcer development has not been extensively examined in the medical literature, particularly with regard to the recent emergence of *Helicobacter pylori* infection as a causative agent in peptic ulcer disease. The following case report is unusual in that it is, to our knowledge, the first case report of symptomatic gastric sarcoidosis mimicking peptic ulcer disease and confounded by *Helicobacter pylori* infection.

Case Report

A 40-year-old woman with a medical history of pulmonary, ocular, hepatic, and biopsy-proven cutaneous sarcoidosis diagnosed in 1993, non-insulin-dependent diabetes mellitus, congestive heart failure, hypertension, and peptic ulcer disease complained in June 1995 of recurrent epigastric pain, intermittent hoarseness, and dysphagia for approximately 1 year. She said she had occasional pyrosis and reflux of food and liquids as well as persistent postprandial nausea with occasional emesis. She denied hematemesis or melena. The patient had been taking ranitidine sporadically, which had provided minimal relief of her symptoms. She had had a 10-pound weight loss during the preceding 12 months. She had no history of fever, chills, chest pain, pancreatitis, hepatitis, gallbladder disease, change in bowel habits, or urinary tract symptoms. Nor had she been exposed to tuberculosis. She denied any use of alcohol or illegal drugs, but she did smoke a half-pack of cigarettes per day. She was not taking any nonsteroidal anti-inflammatory medications.

On physical examination she was an obese patient in no acute distress. Her temperature, blood pressure, and pulse were all within normal range. Her lungs were clear to auscultation and percussion, and findings on a cardiac examination were normal. On abdominal examination she had moderate supraumbilical pain to deep palpation, but no rebound or guarding, and there was no palpable hepatosplenomegaly or mass. Extremities were without clubbing, cyanosis, or edema. There was no palpable lymphadenopathy.

The patient had been seen for similar complaints approximately 8 months earlier. The workup at that time included a barium swallow, esophagogastroduodenoscopy (EGD), and nasopharyngoscopy. The barium swallow was interpreted as normal. An EGD performed in November 1994 showed prepyloric gastric erosions, diffuse antral and fundic gastritis, and nonerosive esophagitis. A test for *Campylobacter*-like organ-

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Table 1. Summary of Case Reports of Symptomatic Gastric Sarcoidosis, 1984-1996.

Author, Year	Age	Sex	Symptoms	Other Organs (Biopsy)	Gastric Involvement
Gallagher et al, 1984 ⁵	18	M	Dyspepsia	Supraclavicular lymph nodes	Gastritis
Tinker et al, 1985 ⁴	22	F	Abdominal pain, vomiting, weight loss, diarrhea	Esophagus, duodenum, rectum, appendix, thyroid	Not reported
Croxon et al, 1987 ¹³	25	F	Epigastric pain, vomiting, weight loss	Liver, lymph nodes	Prepyloric ulcer
Bellan et al, 1988 ¹¹	44	M	Indigestion, nausea, vomiting, weight loss	Lung, lymph nodes	Midbody ulcer
Panella et al, 1988 ¹⁴	61	F	Hematemesis	Lung	Prepyloric ulcer
Levine et al, 1989 ¹⁵	70	M	Epigastric pain, anorexia, nausea, weight loss	Not reported	Gastritis
George et al, 1992 ¹⁶	35	M	Nausea, vomiting, weight loss, anorexia	Liver	Mucosal thickening
Roth et al, 1994 ¹⁷	31	M	Abdominal pain, nausea, vomiting, weight loss	Eye, skin	Pyloric channel ulcer, gastritis
Pope and Danford, 1996	40	F	Epigastric pain, dysphagia, nausea, vomiting, pyrosis	Skin	Prepyloric erosions, gastritis

isms from samples obtained at endoscopy from the antrum was positive for *Helicobacter pylori*. Gastric biopsies revealed acute and chronic inflammation, edema, and spiral organisms consistent with *H pylori*. A nasopharyngoscopy showed aphthous ulcers anterior to the vocal cords. A diagnosis of peptic ulcer disease with gastroesophageal reflux disease and reflux-associated laryngitis was made. Standard *H pylori* antimicrobial therapy (bismuth sulfate, metronidazole, and amoxicillin) was prescribed for 14 days and ranitidine was prescribed twice daily for symptom relief. At a 6-week follow-up visit, she reported mild improvement in her symptoms.

After a recurrence of symptoms in June 1995, ranitidine was discontinued, and the patient was prescribed omeprazole, 20 mg each day. The patient returned for follow-up in 6 weeks without any noticeable improvement. An EGD repeated in October 1995 showed patchy erythema with friability in the duodenal bulb and antral erythema with superficial erosions in the prepyloric region and on the lesser curve. The esophagus was normal. Multiple antral biopsies were interpreted as chronic inflammation with several poorly formed noncaseating epithelioid granulomas in the lamina propria, consistent with sarcoidosis. No spiral organisms, fungi, foreign bodies, or acid-fast organisms were seen on special

stained sections. A test for *Campylobacter*-like organisms was negative. A third EGD in November 1995 revealed diffuse mucosal erythema with nodular formations and superficial erosions in the prepyloric antrum. Biopsies of the cardia, antrum, duodenal bulb, and second portion of the duodenum showed chronic inflammation throughout, and granulomatous inflammation consistent with sarcoidosis were found in the antrum only. The antrum biopsies taken from erosion sites consisted of poorly formed granulomas of epithelioid histiocytes with occasional multinucleated giant cells. Once again, acid-fast bacilli and fungal stains were negative, and no *H pylori* was identified. Erythrocyte sedimentation rate at that time was minimally elevated at 21 mm/h.

The patient continued to have symptoms despite twice-a-day omeprazole therapy, so prednisone, 20 mg/d, was prescribed for 4 weeks. The patient's symptoms markedly decreased after 1 week of therapy and had completely resolved by 4 weeks. Prednisone was discontinued at that time because of resolution of symptoms and elevation of the patient's plasma glucose levels. When she was seen for follow-up care 1 month later, she had no recurrence of gastrointestinal symptoms. Sedimentation rate, complete blood count, and serum glucose were within the normal range.

Discussion

Chinitz et al³ reported 20 well-documented cases of symptomatic gastric sarcoidosis in a literature review up to 1984. Their inclusion criteria included evidence of an idiopathic systemic granulomatous disease, symptoms of gastric involvement, and pathologic demonstration of noncaseating granulomata in the stomach. Since their report there have been at least 8 additional cases of symptomatic gastric sarcoidosis published in the English literature that fulfill those criteria. Those cases are outlined in Table 1.

Our case exhibits the complexity that can accompany the evaluation and management of peptic ulcer disease in a patient with sarcoidosis. It is unclear whether this patient's gastric ulceration and symptoms were the result of *H pylori*-mediated peptic ulcer disease, gastric sarcoidosis, both, or neither. *H pylori* is regarded as a causative factor in both duodenal and gastric ulcers, accounting for more than 70 to 90 percent of gastric and 90 to 95 percent of duodenal ulcers.¹⁸⁻²⁰ Typically, eradication of the *H pylori* infection results in the ulcers healing and a reduced recurrence. In this case, the patient's failure to improve clinically and histologically after *H pylori* eradication and vigorous acid-suppression therapy, coupled with a negative history of nonsteroidal anti-inflammatory medication use and subsequent improvement on steroid therapy, suggests that sarcoidosis was at least a major cofactor in the disease process, if not the cause. Infection with *H pylori* does not necessarily result in peptic ulcer disease or symptomatology.²¹ Although the initial antrum biopsies, which showed chronic inflammation and *H pylori*, did not show granulomatous changes, it is uncertain whether sarcoid granulomas were indeed present at the initial EGD and simply not found on those particular biopsies.

It is possible that the *H pylori* infection was not eradicated. Omeprazole therapy has been found to increase the false-negative rate of detection for *H pylori*.²¹ Also, the definite absence of chronic antral gastritis firmly excludes *H pylori* infection, and resolution of antral gastritis was never shown in this case.²² Multiple gastric biopsies and two separate tests for *Campylobacter*-like organisms were negative for *H pylori* organisms, however, making a false-negative detection unlikely in this case. It is not known whether the patient experienced histologic or endoscopic cure after steroid therapy, as

no further endoscopic investigation was undertaken. Treatment of gastric sarcoidosis with steroids has been reported in the literature to result in dramatic clinical responses in up to two thirds of symptomatic cases, although this is not always accompanied by histologic improvement.^{3,23}

The diagnosis of gastric sarcoidosis is dependent upon clinical and histologic evidence of disseminated sarcoidosis and the exclusion of other causes of granulomatous disease, such as histoplasmosis, tuberculosis, syphilis, talcosis, berylliosis, and regional enteritis. The symptoms associated with gastric sarcoidosis (epigastric pain, nausea, vomiting, anorexia, pyrosis, gastrointestinal bleeding, weight loss³), when present, are probably related to the mucosal ulceration in the overlying mucosa or the narrowing of the gastric lumen and outlet because of granulomatous infiltration of the gastric wall. The actual pathogenic mechanism has not been clearly defined, however. Noncaseating sarcoid granulomas have been found within gastric ulcer sections and within the surrounding tissue adjacent to ulcers,^{6,8,9} but sarcoidosis does not characteristically cause ulcers in other affected organs. It is unclear how often granulomas ulcerate,²³ or whether the occurrence is coincidental, as Fung et al⁷ believe. Similarly, the exact mechanism by which *H pylori* causes peptic ulceration is not understood. It is not known whether a relation exists between the *H pylori* infection and the formation of the mucosal granulomas or what, if present, the extent of that relation is.

Gastric sarcoidosis should always be considered in patients who have symptoms of dyspepsia and evidence of sarcoidosis in other organ systems regardless of whether they have a history of peptic ulcer disease. Endoscopy and gastric biopsy are indicated to establish the diagnosis, and steroid therapy might result in healing cases refractory to standard ulcer therapy.

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