A case of Ménétrier’s disease localized to the gastric antrum without helicobacter infection or hypoalbuminemia

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A B S T R A C T
INTRODUCTION: Ménétrier’s disease (MD) is a rare gastric disorder closely associated with Helicobacter pylori infection characterized by enlarged gastric mucosal folds and hyperplasia of surface mucus-secreting cells classically localized to the gastric body. This disease has significant morbidity and mortality secondary to hypoproteinemia, gastric obstruction, hemorrhage, and increased risk of adenocarcinoma.

PRESENTATION OF CASE: We report a 53-year-old female who presented with severe epigastric pain, anorexia, weight loss, and prandial vomiting with serum albumin and chloride levels in the normal range. After serial upper endoscopy with biopsy identified nonspecific inflammatory changes in the absence of H. pylori, surgical exploration was performed with intraoperative tissue samples revealing nondysplastic, foveolar hyperplasia. Gastric antrectomy was performed with gross and microscopic examination verifying the diagnosis of MD.

DISCUSSION: The unusual presentation of this case differentiates it from other known cases due to the rare localization of the disease to the gastric antrum, the absence of H. pylori infection, and the uncharacteristically normal serum albumin level on presentation.

CONCLUSION: This case may represent an unreported subset of MD where limited surgical resection is demonstrated to offer an exceptional outcome.

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1. Introduction

Ménétrier’s disease, also referred to as protein-losing hypertrrophic gastropathy, is a rare condition affecting mostly middle-aged males characterized by hypoproteinemia, hypochloremia, considerable gastric hypertrophy, and increased risk of gastric adenocarcinoma. The etiology of MD is largely unknown, but recently it has been shown that an upregulation of TGF-α binding to gastric epidermal growth factor receptor (EGF-R) is associated with MD and may be the underlying cause of most, if not all, of the cellular changes.

Histologically, this disease is characterized by hyperplasia of the resident mucus-secreting surface cells found in the gastric pits, called foveolar epithelium, which replace much of the normal glandular architecture. These changes are overwhelmingly localized to the gastric body, with close association to colonization of this area with Helicobacter pylori, which normally has a preference for the gastric antrum. The classic clinical presentation of MD includes epigastric pain, non-dependent edema, and signs of chronic obstruction—notably nausea, vomiting, anorexia, and weight loss. The diagnosis is rarely made from presentation alone and requires an appropriate workup including serum albumin levels, upper endoscopy, and biopsy with staining for H. pylori.

Without adequate therapy, this disease has significant morbidity and mortality secondary to gastric obstruction, hemorrhage, progression to cancer, and loss of protein through increased gastric mucosal permeability. Treatment for this rare disease is poorly understood and requires a careful review of the literature where several therapeutic options are explored including H. pylori eradication, somatostatin analog injections, monoclonal antibody therapy, or total/near-total gastric resection.

2. Presentation of case

A 53 year old postmenopausal female with an uncomplicated medical history presented with a four-week history of worsening epigastric pain, bloating, early satiety, and vomiting with intake of solids or liquids resulting in an 18-pound weight loss since symptom onset. With suspected peptic ulcer disease, an esophagogastroduodenoscopy (EGD) was performed with findings of thickened folds and discontinuous inflammatory tissue (Fig. 1). Numerous tissue fragments were obtained for biopsy, which revealed non-malignant, surface epithelial erosion and reactive epithelial changes. The tissues sampled were carefully examined...
for *H. pylori* with no findings of the organism. Following a precipitant return to the emergency department with worsening symptoms, abdominal CT with IV contrast identified gastric wall thickening with no associated gastric mass or adenopathy. A subsequent EGD was performed where biopsied samples from various regions of the stomach demonstrated chronic inflammation, ulceration and intramural microscopic abscesses localized in clusters throughout the antral mucosa. All samples were stained and carefully inspected for *H. pylori* with negative findings.

With an obscure clinical picture, a full surgical workup was performed where labs revealed normal gastrin and CEA tumor marker levels with CBC, LDH, and LFT levels all within the normal range including an albumin of 3.90 g/dL. These labs essentially ruled out Zollinger-Ellison syndrome, lymphoma, and other suspected gastric malignancies. With worsening abdominal pain, nutritional deprivation, and an unclear diagnosis, the patient was prep for an open surgical survey of the abdomen.

Surgical exploration revealed localized thickening and inflammatory changes over the surface of the gastric antrum extending onto the lesser curvature and posterior gastric wall with marked gastric outlet obstruction. With no signs of inflammatory spread or metastasis, the gastric antrum was resected with 1.0 cm margins. Intraoperative biopsy of the resected tissue was sent to pathology where microscopic examination revealed generalized thickening of the muscular wall with areas of scant mucosal inflammation immediately transforming to areas with marked foveolar hyperplasia, microulcerations, considerable submucosal edema and acute inflammatory changes in the absence of significant eosinophilia (Fig. 2). Both the proximal and distal margins of the resection were uninvolved. Careful inspection for dysplasia or *H. pylori* in all aspects of the resected tissue was performed with no associated findings.

With pathological reports that the antral resection contained the localized disease process with negative margins, anastomosis of the proximal gastric antrum and the duodenum was performed without complication.

The patient tolerated the procedure well and began introducing solid food into her diet on post-operative day five without difficulty. She is now in full recovery and enjoying a normal diet with no epigastric pain or signs of anastomotic leakage/obstruction.

![Fig. 1. EGD of the distal stomach showing markedly thickened gastric folds, erythema, and nodularity involving the gastric antrum.](image)

![Fig. 2. Histology from a section of the gastric antrum revealed marked foveolar hyperplasia involving the full thickness of the mucosa.](image)

3. Discussion

This case differentiates itself from others due to the initially normal serum albumin level, the localization of the gross and histological changes to the gastric antrum, and the lack of *H. pylori* colonization. This unusual presentation draws attention to the diagnostic specificity of generally understood principles of the disease process, particularly the occurrence of *H. pylori* infection and serum albumin levels.

*H. pylori* is closely associated with adult MD and has become regarded by some as a precursor to the disease process. A prominent case series investigating 138 patients with hypertrophic gastropathy reported more than 90% of cases having biopsy proven *H. pylori* infection. One hypothesis is that *H. pylori* may induce COX-2 mediated down-regulation of apoptosis in the mucin-secreting gastric cells allowing for hypertrophic changes and severe protein and chloride secretion. A literature review reveals few diagnoses of MD in the absence of *H. pylori* colonization to the affected tissue. Considering the extent of tissue biopsied in this case, great confidence can be made in reporting the negative *H. pylori* status. This offers evidence that *H. pylori* may not be a precursor infection, but rather a possible contributing factor to the development of foveolar hyperplasia and gastric hypertrophy.

Hypoalbuminemia is generally considered to be a defining lab finding for MD. A case series studying a group of adults diagnosed with MD reported a mean serum albumin of 1.8 g/dL (range 1.5–2.3 g/dL) with coexisting edema present in 50% of those studied. In this case, the patient had a serum albumin level of 3.9 g/dL and no edema. It was not until the patient was recovering from surgery that she developed hypoalbuminemia with a trough of 2.6 g/dL. The author believes that the coinciding hypoalbuminemia correlates to prior starvation compounded with a dilutional effect from extensive postoperative hydration; however, it must be considered that this hypoalbuminemia may represent delayed gastrointestinal protein loss in conjunction with the features previously mentioned. Moreover, even with the consideration of compounding factors, the serum albumin trough in this case was higher than the range reported, offering speculation that the pathology was discovered earlier than most reported cases or that this may be a novel subtype of hypertrophic gastropathy.

Treatment for MD is largely divided into schemas that target eradication of *H. pylori* with antisecretory and antibiotic therapy, modulation of the TGF-α/EGF-R signal cascade with the somatostatin analog ocreotide, EGF receptor-binding monoclonal antibody
therapy, or surgical resection. Several studies have been aimed at treating the disease with antisecretory and antimicrobial combination therapy with positive findings, yet in the condition of H. pylori negative MD, one might expect the disease to be refractory to this combination therapy. Anecdotal evidence for ocreotide therapy has been largely aimed at alleviating symptoms associated with the disease, but does not address the concerns for disease progression and gastric adenocarcinoma. Monoclonal antibody therapy targeting EGF receptors has shown promising results for chronic cases; however, surgical resection is the preferred treatment for cases refractory to medical management, acute clinical decline, and for prophylaxis against gastric adenocarcinoma. To date, the standard surgical treatment for MD is total to near-total gastrectomy with the use of laparoscopic technique recently pioneered. Total gastrectomy has largely been performed despite the characteristic antral sparing in MD due to concern for postoperative leakage after anastomosis of inflamed tissue. To the author’s knowledge, no research has been done to analyze the success of limited gastric resection in cases of MD localized to the gastric antrum. This case report, however, demonstrates that in such circumstances, the inflammation may be well circumscribed, potentially allowing diminished rates of complication from anastomotic leakage and overall improved success with limited gastric resection.

In cases of MD, it is unknown whether limited gastrectomy will influence the rate of impending gastric adenocarcinoma. It is conceivable, nevertheless, that resection of all affected tissue in a well-localized disease will dramatically decrease the risk for dysplastic events. This should be considered when evaluating potential therapies for patients with MD.

4. Conclusion

This case may represent a subtype of MD that presents in the adult gastric antrum without H. pylori infection or initial hypoalbuminemia, mimicking advanced ulcerative disease with nutritional depletion and nonspecific pathological findings.

Considering that H. pylori generally colonizes the gastric body in MD localized to this region, H. pylori negative MD may have a higher rate of antral involvement.

Suspicion should be raised with acute gastric obstruction and findings on upper endoscopy of enlarged gastric folds despite H. pylori status for a possible new subtype of MD where limited surgical resection with negative margins may offer the best outcome.

Conflict of interest

None.

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None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Authors contributions

Adam R. Sweeney is the author of this report and main contributor of intellectual content and Maureen K. Lynch is the surgeon, report editor, and contributor of intellectual content.

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