Menetrier’s Disease in a HIV Positive Male
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Abstract

Menetrier’s disease is a rare form of protein-losing gastropathy characterized by giant gastric folds, hypoalbuminemia and achlorhydria. The etiology is unclear although infections like helicobacter pylori and cytomegalovirus have been implicated in some cases. We report a case of 43-year-old male with human immunodeficiency virus who was diagnosed with Menetrier’s disease. This appears to be the first such case described in the literature with these two coexisting conditions. The patient had no evidence of infection with either Helicobacter pylori or cytomegalovirus. He continued to remain symptomatic especially with persistent weight loss and underwent total gastrectomy with excellent clinical response. The present report describes the clinical features, endoscopic, operative and histological findings, and response to total gastrectomy. We discuss the causes of Menetrier’s disease and raise the possibility of human immunodeficiency virus having a potential causal association with the disease. (J Dig Endosc 2010;1:22-25)

Key words: Menetrier’s disease, Human immunodeficiency virus, total gastrectomy, Helicobacter pylori

Case Report

A 43-year-old African American male with human immunodeficiency virus (HIV) infection on HAART was evaluated for complaints of abdominal pain, nausea, vomiting, anorexia and weight loss of 10 pounds in a month. He described his pain as a dull ache in the left periumbilical area which radiated to the left upper quadrant. He denied any gross gastrointestinal bleeding, change in bowel habits, fever or jaundice. His last CD4 count was 137 cells/mm³ and the viral load was 147,500 copies/ml. The past medical history was also significant for similar complaints a year ago which had subsided with Proton Pump Inhibitor therapy for few weeks. He was maintained on HAART regimen, which included Reyataz, Epivir, Norvir and Viread. Physical examination was unremarkable except for some mild deep tenderness in the epigastric region.

The laboratory data showed normal hematocrit, normal hepatic enzymes and renal panel. The serum amylase and lipase levels were also normal. The total serum albumin was 3.6g/dl with total protein of 7.7 g/dl (albumin-globulin ratio of 0.98). Esophagogastroduodenoscopy (EGD) showed evidence of diffuse and marked hypertrophy of the gastric folds associated with limited distensibility with air insufflation, which was much more pronounced in gastric body and fundus (Fig. 1). Multiple biopsies were obtained from the gastric body. On histopathologic examination there

Figure 1: Endoscopic view of large gastric folds in body and fundus

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was marked edema with no evidence of Helicobacter pylori (H. Pylori).

Due to persistent symptoms with no identifiable cause on superficial gastric mucosal biopsies, a repeat EGD with endoscopic ultrasound (EUS) was performed. Again diffuse, hypertrophic and thickened gastric folds were noted in the body of the stomach with antral sparing along with poor distensibility of the entire proximal stomach. Multiple large particle cold biopsies were obtained including a large forceps biopsy from the gastric folds and the intervening gastric mucosa. EUS confirmed the diffuse wall thickness of the gastric folds in the fundus, greater curve and the body of the stomach which appeared to originate from the mucosa and extended into the submucosal. The histopathologic examination showed mixed cellular infiltrates and one of the biopsies had predominant lymphocytes with eosinophils and glandular degeneration. There was no evidence of H. Pylori, cytomegalovirus(CMV) or fungal infections. Serology was also negative for H. Pylori. CT scan of abdomen with contrast showed marked diffuse thickening of the stomach wall (Fig. 2).

The patient continued to remain symptomatic with nausea, vomiting and weight loss. His albumin dropped from 3.6g/dl to 2.7g/dl over three months. He was also becoming anemic with hemoglobin of 7.1 g/dl and hematocrit of 24.3% with an MCV of 75.3 fl and serum iron of 4 microgram/dl. A full thickness gastric biopsy was obtained laproscopically and it showed markedly diffuse foveolar hyperplasia with glandular atrophy consistent with Menetrier’s disease. Following this diagnosis he was started on a high protein diet and continued on Proton Pump Inhibitor. However, his symptoms persisted and a total gastrectomy was performed. On gross examination, the surgical specimen of his stomach measured 25 x 17cms with a wall thickness of 2.5cms and weighed about 960.8 grams. The gastric fold had a cerebriform thickened appearance and it almost involved the entire stomach (Fig. 3 and Fig. 4) On histology, the mucosa showed foveolar hyperplasia and glandular atrophy (Fig. 5).

His symptoms slowly resolved after the surgery and he was started on iron and monthly vitamin B₁₂ supplementation. He was also placed on low lactose and low fat diet. His albumin improved to 3.9 g/dl and his anemia resolved with iron supplementation with noticeable improvement in weight. He continues to do well and is asymptomatic.
Manetrier’s Disease

Discussion

This disease was first described by Menetrier in 1888 as “polyadenoma en nappe” or multiple sheet-like adenomas. It is categorized as a hyperplastic gastropathy and has to be differentiated from other conditions with giant folds and epithelial hyperplasia like hypertrophic lymphocytic gastritis and Zollinger-Ellison Syndrome. The distinction between these conditions cannot be made by gross examination alone. Histologically Manetrier’s disease has classic findings of foveolar hyperplasia with cystic dilation of glands. Wolfsen et al made the histological distinction between lymphocytic gastritis and Menetrier’s disease and observed that patients with hypertrophic lymphocytic gastritis have severe inflammation with numerous lymphocytic infiltration and mild foveolar hyperplasia whereas Menetrier’s disease is characterized by minimal infiltrates with significantly thicker mucosa and marked foveolar hyperplasia (1). Zollinger-Ellison Syndrome is characterized by increase in the gastrin producing parietal cells causing increased acid production with no change in the surface foveolar cells. Our patient had the classic macro and microscopic findings of Menetrier’s disease as seen in Fig. 4 and Fig. 5.

The cause of Menetrier’s disease has not been well established but it has been known to be associated with infections like CMV and H. pylori. It is believed that H. pylori increases IL 1 beta and hepatocyte growth factor (HGF) production in the gastric mucosa causing enlarged gastric folds (2). The association is limited to case reports of patients with resolution of the disease by eradication of H. pylori (3-7). Unlike H. pylori, infection with CMV has been well associated with Menetrier’s disease of childhood, a transient process seen in acute infection with CMV. It usually follows a benign course and resolves on its own (8, 9). Adult patients with Menetrier’s disease are not commonly infected with CMV although there have been few reports of immunocompetent adults with CMV associated Menetrier’s disease (10,12). The immunostaining of the gastric mucosa of these patients with CMV has shown over expression of TGF-alpha (transforming growth factor alpha) (10-12). TGF-alpha is an epithelial cell mitogen which increases the gastric mucin content and inhibits acid production. It takes part in the reparative function of the gastric mucosa after injury and some triggers might lead to overexpression of this growth factor. Studies in human and mouse model have shown that over expression of TGF-alpha in the gastric mucosa can lead to foveolar hyperplasia and atrophy of parietal cells which is the typical finding in Menetrier’s disease (13-15). It is not known if CMV directly acts as a trigger for the increase in the TGF-alpha levels but these studies strongly suggest that CMV causes Menetrier’s disease especially in children (10-15).

Our patient was negative for both CMV and H. pylori but this raises a question if HIV could cause Menetrier’s disease. We do not know if TGF-alpha is increased in the gastric mucosa in association with HIV. In our literature search we found evidence that HIV-1 TATgene expression can increase the transcription of TGF-alpha in a EGF (Epidermal Growth Factor) dependant manner (16). EGF is usually increased in the gastric mucosa during the repair of acute and chronic mucosal injuries and ulcers (17). There is a possibility that HIV gene causes overexpression of TGF-alpha, a growth factor which might be increased in the gastric mucosa of these patients either secondary to the viral infection or other mucosal injuries.

In summary we report a patient with HIV who was diagnosed with Menetrier’s disease and we postulate a causal association between HIV and Menetrier’s disease.

References


