Menetrier's Disease Presenting with Iron Deficiency Anemia*

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ABSTRACT

Menetrier's disease (MD) or polyadenomes en nappe is a form of hypertrophic gastropathy occurring primarily in middle-aged males. Patients generally present clinically with dyspepsia and, on occasion, with hypoproteinemie edema and anemia. The latter feature, when combined with the radiographic appearance of the stomach in MD, can lend to confusion with carcinoma and malignant lymphoma. To illustrate this diagnostic problem, a case is reported of a 41-year-old female who initially presented to her family physician with symptoms of easy fatigue and dyspnea on exertion and signs of pallor and ankle edema. Pertinent laboratory findings included a hemoglobin of 2.8 g/dL, hematocrit of 10.3 percent, mean corpuscular volume of 63.4 µ³, a serum albumin of 2.7 g/dL, and heme positive stools. Endoscopic examination revealed a circumferential polypoid mass involving the cardia and fundus of the stomach with relative sparing of the antrum. A CT scan of the abdomen and pelvis showed a large mass in the stomach which the radiologists and gastroenterologists believed probably represented a lymphoma or gastric carcinoma. A total gastrectomy specimen exhibited features of MD. Routine bright-field microscopy and immunohistochemical reactivity for transforming growth factor-alpha confirmed the diagnosis of MD. Moreover, ulceration of the tips of some of the hypertrophied gastric folds provided an explanation for the iron deficiency anemia. Awareness that MD may present with anemia will help in the differential diagnosis with lymphoma and carcinoma.

Introduction

Pierre Menetrier wrote a treatise in 1888 discussing glandular hypertrophy of the stomach, which he termed polyadenomes en nappe, and its possible relationship to gastric carcinoma. Since that time, there have been many case reports and case series published that have grouped diverse syndromes having giant gastric folds together under the general term "Menetrier's disease," often without a histologic diagnosis or defined criteria. The currently accepted criteria for Menetrier's disease require the presence of enlarged gastric folds, specific histopathological features including surface epithelial hyperplasia and glandular atrophy of the gastric body mucosa, and hypoproteinemie. Hypochlorhydria
and increased gastric mucus production are also common. Menetrier’s disease, as currently defined, is a rare entity that in adults occurs primarily in middle-aged males. Very few case series have documented presenting symptoms or concurrent physical findings. A patient is described with Menetrier’s disease who initially presented with a profound iron deficiency anemia.

Case Report

A 41-year-old female presented to her family physician in July, 1996, complaining of easy fatigue, dyspnea on exertion, palp, and ankle edema. A complete blood count (CBC) at that time included a hemoglobin of 2.8 g/dL, hematocrit of 10.3 percent, and mean corpuscular volume (MCV) of 63.4 mc. She was immediately admitted to a local hospital for transfusion. Additional laboratory findings at this time included a serum iron of 4 mcg/dL, total iron binding capacity (TIBC) of 301 mcg/dL, and serum albumin of 3.1 g/dL. A thyroid stimulating hormone (TSH) level was mildly elevated at 6.69 mcIU/mL. Chest x-ray and upper abdominal ultrasound studies were unremarkable. She was discharged the following day and instructed to begin iron and folate dietary supplements, as well as synthroid.

She returned to her family physician in September complaining of a "lump" in her belly, predominantly left-sided abdominal cramping, early satiety, and occasional vomiting. She denied diarrhea, constipation, weight loss, hematemesis, melena, or change in appetite. No discrete abdominal mass could be palpated, but there seemed to be a fullness in the upper abdomen. She had prebital edema. Her stool was heme-positive.

In October, she underwent an upper endoscopic procedure which showed a circumferential, polypoid mass involving the cardia and fundus of the stomach with relative sparing of the antrum (figure 1). Gastric biopsy findings were consistent with a hypertrophic gastropathy. A CT scan of the abdomen and pelvis the following week showed a large irregular mass in the stomach suspicious for gastric carcinoma or lymphoma (figure 1). A calcified splenic artery aneurysm was incidentally discovered. The radiographic and endoscopic features combined with the profound anemia presented a diagnostic dilemma, suggesting a gastric carcinoma or malignant lymphoma.

Anemia has been reported previously in association with Menetrier’s disease in three of 10 patients seen at the Mayo Clinic; however, the anemia was not further characterized. What are the possible mechanisms of iron deficiency in this patient? It is believed there are four possible mechanisms that may have played a role in this case. First, the patient's dietary habits are not documented in the chart, but this must be considered. Second, the tips of some of the folds were necrotic (figure 2). Immunohistochcmical staining for transforming growth factor alpha (TGFα) demonstrated enhanced basolateral staining of the foveolar epithelium. The case was diagnosed as hyperplastic gastropathy consistent with Menetrier’s disease.

Discussion

This case has all the typical features of Menetrier’s disease. In addition, the patient presented with a profound iron deficiency anemia. The radiographic and endoscopic features combined with the profound anemia presented a diagnostic dilemma, suggesting a gastric carcinoma or malignant lymphoma. Although the original biopsy was diagnosed as hypertrophic gastropathy, the possibility of carcinoma still existed since 10 to 15 percent of reported cases of Menetrier’s disease have also developed gastric carcinoma. Owing to the extensive gastric mucosal involvement, adequate sampling to exclude carcinoma would be impossible.
in hypoproteinemia that leads to peripheral edema and even anasarca. Such protein loss would include transferrin, the major carrier protein needed for absorption of dietary iron from the intestinal lumen.

The final possible mechanism for iron deficiency in this case involves changes in the gastric secretions in Menetrier's disease. Most patients have decreased gastric acid production owing in part to atrophy of the gastric
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Figure 2. (A) Gross photograph showing mucosal surface of stomach with sparing of antrum (upper right corner); hematoxylin and eosin stained sections showing: (B) whole mount section of an enlarged gastric fold with a polypoid projection, (C) massive hyperplasia of the foveolar compartment, and (D) focal hemorrhagic necrosis (at 31x).

Mucosal glandular compartment. Most patients are reported to have increased gastric mucus production, resulting in a higher pH of the gastric secretions. Recent evidence suggests that increased production of transforming growth factor alpha (TGFα) plays a significant role in the development of Menetrier's disease. Biological actions of TGFα in the gastrointestinal tract include inhibition of histamine stimulated parietal cell acid secretion, increased mucus production, and cell proliferation. The end result of these various factors is a rise in gastric secretion pH. A low gastric pH is necessary for absorption of non-heme dietary iron so that ferric iron can be reduced to the more soluble and stable ferrous state, then chelated and absorbed. A low pH also helps denature proteins, releasing bound iron which can then be reduced and absorbed.

In summary, this case serves to remind us that a gastric mass and anemia do not always
indicate malignancy. Menetrier’s disease provides multiple pathophysiologic mechanisms to account for such a presentation.

References