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CASE REPORT

Ménétrier's disease: Long-term remission with lanreotide

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Summary Ménétrier's disease is a rare hypertrophic gastropathy, causing protein leak. An overexpression of transforming growth factor alpha is involved. In inhibiting the epidermal growth factor receptor, cetuximab and somatostatin analogues are the two most promising treatments, allowing to avoid radical gastrectomy. We report the case of a patient with a sustained clinical remission after treatment with lanreotide, but without complete endoscopic healing. We discuss the available therapeutic options and present a literature review of somatostatin analogues for the treatment of Ménétrier's disease.

Introduction

Ménétrier's disease, also called hypoproteinemic hypertrophic gastropathy, is a rare disorder of gastric mucosal growth. Histological findings include giant hypertrophic folds with marked foveolar hyperplasia, atrophy of glands and an increase in mucosal thickness. Symptoms of Ménétrier's disease are severe epigastric pain, nausea, vomiting, anorexia, weight loss and edema. Others features are a loss of proteins with frequent hypoalbuminemia, excessive mucus secretion, decreased gastric acid secretion with normal or slightly elevated serum gastrin levels. Several cases of Ménétrier's disease with gastric cancer have been reported but no statistical risk association has been shown

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[1]. Gastric polyps, polyposis syndromes and hyperplastic gastritis due to *Helicobacter pylori* infection can mimic Ménétrier's disease [2].

The etiology is not well known, although the disease seems to be associated with cytomegalovirus in children, and rare familial forms have been described [3,4]. Based on studies performed in transgenic mice and humans, an increased expression of transforming growth factor alpha (TGF-α) was shown [5,6]. In inhibiting the epidermal growth factor receptor (EGFR), cetuximab and somatostatin analogues are the two most promising treatments in Ménétrier's disease, allowing to avoid radical gastrectomy [7,8].

We report a well-documented case of Ménétrier's disease in a 56-year-old man. One year of treatment with lanreotide led to a clinical sustained remission, but without complete endoscopic healing. Seven years after the end of treatment, endoscopic remission was not achieved, but the patient remained asymptomatic. Highlights are focused on therapeutic options and on the place of somatostatine analogues in the treatment of this disease.

Case report

On February 2006, a 56-year-old man was admitted with a history of significant weight loss and atypical epigastric pain for 2 months. He had no previous medical problem and was regular tobacco-user. Despite 40 mg/day of proton-pump inhibitor (esomeprazole) for 2 weeks, the pain progressed and severe inferior limb edema, moderate pleural effusion and ascites appeared. There was no evidence of right heart failure.

Laboratory tests revealed a serum total protein of 28 g/L (NR 65—85 g/L), with hypoalbuminemia (13 g/L, NR 35—46 g/L) and hypogammaglobulinemia (2.27 g/L, NR 8—16 g/L). Proteinuria was negative. Blood count, erythrocyte sedimentation rate, C-reactive protein, serum electrolytes, creatinin, urea, calcium and ferritin were normal. The serum gastrin was 193 μU/mL (NR 28—115 μU/mL). Cytomegalovirus IgM antibodies and *H. pylori* serology were both negative.

Endoscopy revealed giant mucosal folds in the fundus, flimsy with heavy secretion of mucus (Fig. 1) and normal antrum. Endoscopic ultrasonography showed the thickened (8 mm) second layer at the body level, with hypoechogenic mucus cysts, whereas other layers and antral wall were normal. Biopsies of the fundus revealed a thickened mucosa, foveolar hyperplasia with stretched crypts made of tubular glands presenting occasional muciparous differentiation (Fig. 2). They confirmed microcystic structure, but no sign of *H. pylori* was found. Muscle fiber expansions were noted in the lamina propria. Antrum and duodenum biopsies were normal. Regarding these elements, Ménétrier's disease was diagnosed.

Proton-pump inhibitor treatment was increased (esomeprazole 80 mg/day). Several albumin injections were administered, combined with short time use of diuretics (furosemide 40 mg/day) and analgesics. After 1 month, hypoalbuminemia was persistent with medium limbs edema. Pain control was poor. Subcutaneous slow-release lanreotide (Somatuline® LAR 30 mg) was injected,

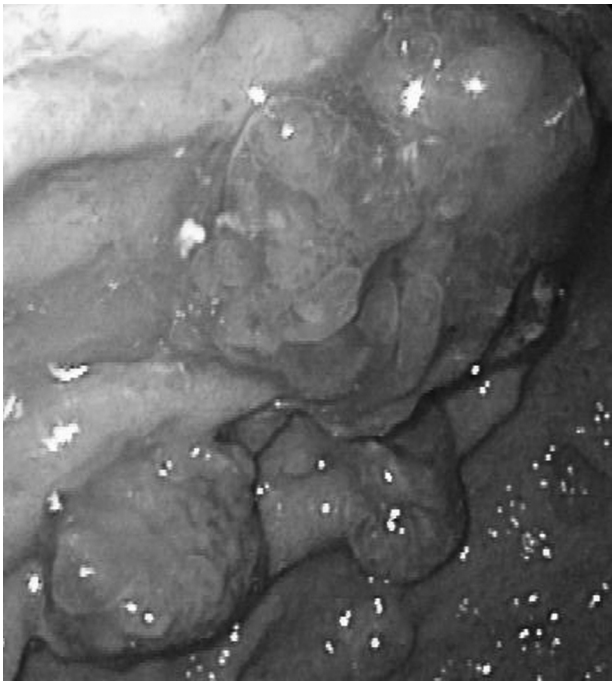

Figure 1 Endoscopy at diagnosis of the Ménétrier's disease. Endoscopy showing giant mucosal folds in the fundus, flimsy with heavy secretion of mucus.

scheduled every 14 days for 6 months, then 60 mg/month for 6 months. Esomeprazole 40 mg was maintained all along.

After 6 weeks of this treatment, analgesics were no further necessary and edema had resolved.

At 6 months, weight was back to normal and albuminemia was normalized (37 g/L). Endoscopy showed significant reduction of the giant fundic folds.

After 12 months of lanreotide, patient was asymptomatic and serum albuminemia was stable at 36 g/L. Endoscopic lesions were unchanged and lanreotide was stopped. Endoscopic control made 7 months after lanreotide interruption showed persistent giant fundic folds, clearly in decrease. Cardia revealed polyp-like structures (5 to 15 mm in size), histologically confirmed as non-dysplastic Ménétrier's mucosa. No pain or Ménétrier's disease associated symptoms were reported.

Yearly controls for 7 years confirmed the absence of symptoms. Endoscopic examination showed persistent thickening of the mucosa in the fundus and body forming giant folds, but still reduced regarding initial diagnosis. MRI enterography confirmed moderate thickening of gastric mucosal folds in the fundus (Fig. 3). *H. pylori* infection was never detected and no carcinomatous transformation occurred. Yearly endoscopic follow-up with gastric biopsies was maintained.

Discussion

The Ménétrier's disease is a very uncommon gastropathy of unknown etiopathology, characterized by a hyperplasia of mucosecretive epithelium, and a protein leakage through gastric mucosa, causing severe hypoproteinemia. Histological findings include giant hypertrophic folds with marked