

Menetrier's Disease in Korea: Report of Two Cases and Review of Cases in a Gastric Cancer Prevalent Region

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Menetrier's disease is a rare disease of the stomach generally described as hypertrophic gastropathy associated with hypoproteinemia. Gastric resection is still the most definitive treatment for the disease, but the appropriate extent of resection has not been determined. One of the major factors that would determine the extent of gastric resection in Menetrier's disease is its malignant potential. We present two recent cases of Menetrier's disease treated in our institution and review cases of the disease reported in Korea where the incidence of gastric cancer is one of the highest in the world.

Key Words: Menetrier's disease, gastrectomy, gastric cancer

INTRODUCTION

Menetrier's disease is a rare disease of the stomach, generally described as hypertrophic gastropathy associated with hypoproteinemia. The clinical presentation as well as the endoscopic and radiographic features of the disease are similar to those of gastric malignancy, hence the need to understand it better.

Nevertheless, no diagnostic criteria for the disease have been established since Menetrier's report in 1888¹ and its etiology remains unknown. Moreover, little agreement has been reached over its management, although surgical resection is still the most definitive treatment, especially for patients with uncontrollable bleeding or protein loss.²⁻⁴ However, surgeons have yet to agree on

the most appropriate type of surgical resection.

One of the major issues in the surgical management of Menetrier's disease is its malignant potential, which would determine the extent of gastric resection. The risk of malignancy in Menetrier's disease, however, is still controversial.⁵⁻⁷ We present two cases of Menetrier's disease recently treated in our institution and review cases of the disease reported in Korea where the incidence of gastric cancer is one of the highest in the world.^{8,9}

CASE REPORT

Case 1

A 47-year-old Korean man with no significant past medical history presented to Yonsei University Medical Center (YUMC) on March 11th, 2002, complaining of a sudden onset vague intermittent low abdominal pain of 2-week duration. The pain was alleviated with food. He denied hematemesis, hematochezia, melena, diarrhea, weight loss, edema, fever, or any other symptoms. He was on no medications and denied having any allergies. His family history was significant for a brother who had a distal subtotal gastrectomy for a well-differentiated adenocarcinoma.

Physical examination revealed a well-developed man with moderate nutritional status and normal vital signs. Mild pitting edema of the lower extremities was noted. The rest of his physical exam, including an abdominal exam, was normal. Laboratory studies were significant for a hemoglobin level of 7.7g/dl, hematocrit of 26.8%, total protein level of 3.7g/dl and an albumin level of 1.4g/dl.

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Computed Tomography (CT) of the abdomen and pelvis showed diffusely thickened gastric folds (Fig. 1). Multiple endoscopic biopsies of the stomach showed hypertrophic mucosa and a tubulovillous adenoma with low grade epithelial dysplasia in the upper body region. The patient remained stable and his symptoms improved with conservative treatment. He was discharged on antacids and iron & folate supplements on March 22nd, 2002.

Follow-up EGD with biopsy on January 8th, 2003 showed intestinal metaplasia in the body and fundus of the stomach. The patient was readmitted to the hospital on February 3rd, 2003 for a diagnostic endoscopic mucosal resection (EMR). Pathology studies of the EMR of a 2 × 1.2 cm polypoid lesion on the upper body of the stomach showed a well-differentiated adenocarcinoma involving the lateral resection margins (Fig. 1).

On March 5th, 2003, the patient underwent total gastrectomy with D2 lymph node dissection, Roux-en-Y esophagojejunostomy, and splenectomy. Grossly, the stomach was enlarged measuring 25 cm along the lesser curvature and 45 cm along the greater curvature. Hypertrophied gastric folds resembling cerebral convolutions were noted (Fig. 2). Enlarged perigastric lymph nodes including those at the splenic hilum were also noted intraoperatively. Histopathologic studies revealed marked mucosal hypertrophy and foveolar hyperplasia with cystic dilatation and confirmed the EMR diagnosis of a well-differentiated adenocarcinoma confined to the mucosa (Fig. 3). The spleen and lymph nodes were free of disease.

The postoperative hospital course was uneventful and total protein and albumin levels improved to 4.2 g/dl and 3.1 g/100 dl, respectively. The patient was discharged home, having tolerated a soft diet on the 7th postoperative day. He has been doing well since discharge and has regained almost all of his usual body weight of 60 kg (currently 56 kg).

Case 2

A 58-year-old Korean man presented to YUMC on April 6th, 2001, complaining of epigastric discomfort of 3-month duration and weight loss of 4 kg over a 2-month period. The patient had no

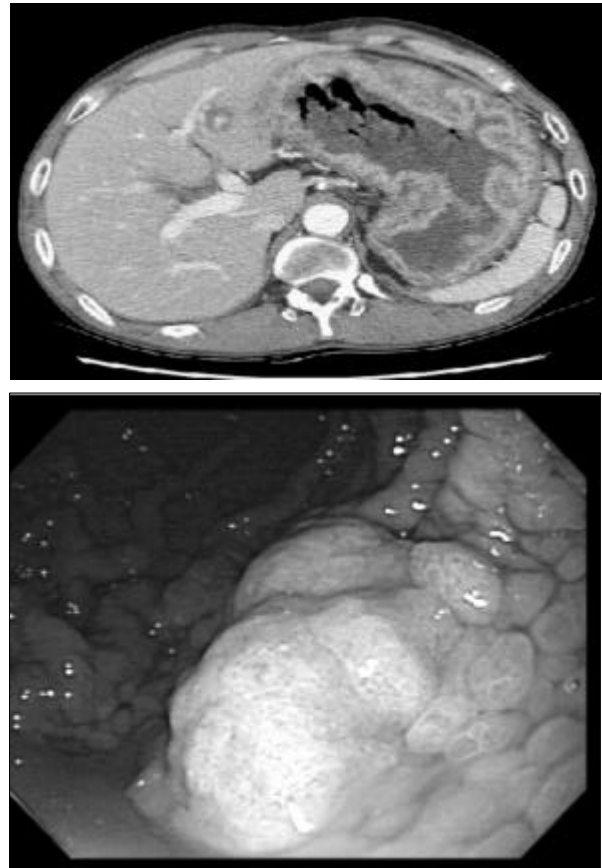


Fig. 1. A. Computed Tomography (CT) of the patient in Case 1 showing markedly enlarged gastric folds. B. Esophagogastroduodenoscopy (EGD) of a polypoid lesion during Endoscopic Mucosal Resection (EMR) of the patient in Case 1. Note the enlarged gastric folds in the background.

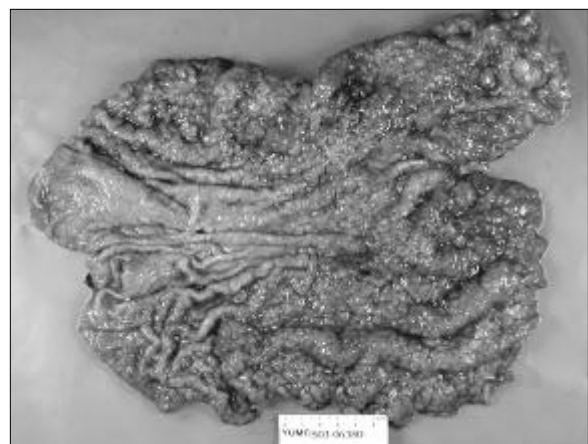


Fig. 2. Total gastrectomy specimen in Case 1 showing enlarged gastric folds sparing the antrum. Arrow shows where a well differentiated adenocarcinoma was diagnosed by EMR.

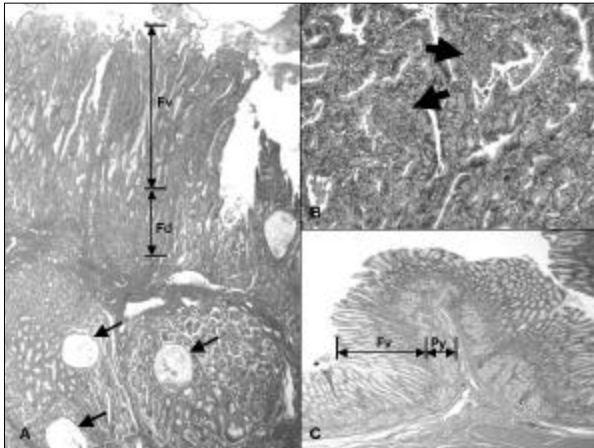


Fig. 3. A. Low power view of the fundic mucosa of the patient in Case 1. The normal foveolar (Fv) gland to fundic (Fd) gland ratio of 1:41 has been reversed due to marked foveolar hyperplasia. Cystic dilatation was also noted (small arrows). B. Well differentiated adenocarcinoma (big arrows) in the fundus of the stomach in Case 1. C. Low power view of the pyloric mucosa of the patient in Case 2. The normal foveolar gland (Fv) to pyloric gland (Py) ratio of 1:110 has been disrupted due to foveolar hyperplasia (Hematoxylin and Eosin. A, $\times 10$; B, $\times 100$; C, $\times 10$).

significant past medical history and was not on any medications. His family and social history were negative for any risk factors. A physical examination, including an abdominal exam, was normal. Vital signs were stable.

An EGD exam showed gastric outlet obstruction due to marked mucosal thickening. CT of the abdomen and pelvis showed diffusely enlarged gastric folds especially at the prepyloric antrum. An upper gastrointestinal (UGI) series with oral barium contrast was a limited study due to "large amounts of secretion from the gastric mucosa." Laboratory studies were within normal limits except for a total protein level of 5.4g/dl and an albumin level of 3.1g/dl.

The patient underwent distal subtotal gastrectomy and Bilroth II gastrojejunostomy on April 10th, 2001 for gastric outlet obstruction and risk of malignancy. A nasogastric tube was left in place after Bilroth II gastrojejunostomy due to concern over the stability of the anastomosis between the hypertrophied gastric mucosa and the normal jejunal mucosa.

Histopathologic studies showed marked mucosal hypertrophy with gastric cystica profunda

formation consistent with Menetrier's disease (Fig. 3) without evidence of malignancy.

The patient had an uneventful postoperative course. Serum total protein levels and albumin levels were 6.2 g/dl and 3.5 g/dl, respectively, on the 6th postoperative day. The nasogastric tube was discontinued on the 7th postoperative day and the patient was discharged home on the 10th postoperative day, tolerating soft diet. The patient has been doing well, tolerating regular diet, and had regained all of his usual weight of 50 kg. There was no evidence of malignancy during the follow-up period.

SELECTION OF CASES IN KOREA

Upon reviewing the Korean literature, we found 20 cases of Menetrier's disease in Korea. The following criteria were used to confirm the diagnosis of Menetrier's disease: (1) the presence of diffusely enlarged gastric folds (2) laboratory evidence of hypoproteinemia, and (3) histologic findings of foveolar hyperplasia.

Nine of the 20 reported cases met our diagnostic criteria. We selected 6 surgical cases¹¹⁻¹⁶ from these 9 cases where a full surgical specimen was available for a definitive pathology study (Table 1). Follow-up information after surgery was obtained by directly contacting the authors of the case reports when necessary.

DISCUSSION

A common problem encountered when studying Menetrier's disease is the lack of universal diagnostic criteria for the disease. In an effort to be consistent in our diagnosis, we applied the diagnostic criteria commonly found in the international literature, namely, (1) the presence of diffusely enlarged gastric folds, (2) laboratory evidence of hypoproteinemia, and (3) histologic findings of foveolar hyperplasia.

Hypertrophic gastropathy can be caused by a variety of disorders such as malignancy, Zollinger-Ellison syndrome, syphilis, sarcoidosis, etc. However, enlarged gastric folds associated with hypoproteinemia and foveolar hyperplasia are

Table 1. Surgical Outcome of Menetrier's Disease Cases in Korea

Case Report	Gender & Age	Pre-op Diagnosis or Reason for Surgery	Pre-op Serum Laboratory Studies	Extent of Gastrectomy	Surgical Outcome & Post-op. follow-up period
Song CE et al. ¹⁰	M/61	Failed medical treatment (50 days)	T. Protein: 3.6g/dl Albumin: 1.6g/dl	total	Complication: malnutrition & pneumonia. Follow-up: 1 month
Hwang KM et al. ¹¹	M/37	Persistent hematemesis	T. Protein: 4.4g/dl Albumin: 2.6g/dl	total	Complication: small bowel obstruction. Follow-up: 1 month
Kim JH et al. ¹²	M/39	Persistent hematemesis	T. Protein: 4.3g/dl Albumin: 2.5g/dl	total	Improved. Follow-up: 54 months
Kang HI et al. ¹³	M/46	Menetrier's disease	T. Protein: 4.4g/dl Albumin: 2.1g/dl	total	Improved. Follow-up: 60 months.
Case1	M/47	Well diff. adenoCA	T. Protein: 3.7g/dl Albumin: 1.4g/dl	total	Improved. Follow-up: 7 months
Kang JC et al. ¹⁴	M/40	Persistent lower GI bleed	T. Protein: 4.0g/dl Albumin: 2.0g/dl	partial	Improved. Follow-up: 1 month.
Lim KC et al. ¹⁵	M/56	Menetrier's disease	T. Protein: 5.4g/dl Albumin: 3.0 g/dl	partial	Improved. Follow-up: 50 months.
Case2	M/58	Gastric outlet obstruction	T. Protein: 5.4g/dl Albumin: 3.1g/dl	partial	Improved. Follow-up: 24 months.

more likely be due to Menetrier's disease than other causes of hypertrophic gastropathy.^{3,5,16,17} Therefore, though it is possible that we have overlooked some cases of Menetrier's disease by applying the above criteria, we feel that the diagnosis in the selected cases is consistent with most reports in the international literature.

Various forms of treatment for Menetrier's disease have been suggested in the international literature, including conservative treatment with high-protein diet, antacids and anti-cholinergics¹⁸ and even monoclonal antibodies against epidermal growth factor receptor.¹⁹ However, surgical resection is still the most definitive treatment for Menetrier's disease, especially for patients with uncontrollable protein loss or bleeding. An obvious question then follows: what should be the extent of gastric resection?

Arguments in favor of total gastrectomy include (1) the difficulty making an anastomosis due to the hypertrophied mucosa of the diseased gastric tissue, (2) the risk of malignancy in Menetrier's disease, and (3) the good clinical outcomes achieved by total gastrectomy.^{20,21} Those in favor of partial gastrectomy claim that extensive gastric resection with its associated morbidity is not necessary in order to control excessive protein loss and/or bleeding in Menetrier's disease.²²

Nevertheless, the standard extent of gastric resection has not been determined yet. In our institution, for example, the extent of gastric resection was dictated by the location of a targeted lesion rather than by the disease itself. Hence, the patient in case 1 underwent total gastrectomy because of a cancerous lesion in the upper body of the stomach whereas the patient in case 2 un-

derwent distal partial gastrectomy for an obstructing lesion in the prepyloric antrum. The fact that the patient in case 2 had enlarged gastric folds throughout the stomach did not affect the extent of gastric resection.

In terms of surgical outcome, patients in both the partial and total gastrectomy groups tolerated the procedure well, except for one patient who had left-sided hemiparesis due to stroke preoperatively.¹² No postoperative complication was noted during the follow-up of patients that received either procedure.

The main concern in the surgical treatment of Menetrier's disease appears to be, then, the malignant potential of the disease rather than the technical feasibility of gastric resection. The risk of malignancy in Menetrier's disease, however, remains controversial.⁵⁻⁷ In their review of eight large series on Menetrier's disease, Simson et al. reported an incidence rate of gastric adenocarcinoma ranging from 0% to 8% among patients with Menetrier's disease.⁷

Out of the 9 cases in Korea that met our criteria for Menetrier's disease, one case (case 1) was associated with gastric cancer. In this case, gastric cancer developed during follow-up after the diagnosis of Menetrier's disease, thus suggesting an increased risk of cancer in Menetrier's disease. However, the possibility of a coincidental malignant development could not be ruled out either. Moreover, no malignant development was observed in the remnant stomach of the two patients who underwent partial gastrectomy. Therefore, it is still premature to suggest an association between Menetrier's disease and gastric cancer at this time.

In conclusion, it is difficult to derive from our experience and review of the Korean cases whether total gastrectomy is more appropriate than partial gastrectomy for the treatment of Menetrier's disease or vice versa. Moreover, the premalignant potential of the disease remains to be determined. Additional large scale studies would be necessary, although such studies would be very difficult to perform and their value questionable given the rarity of the disease. In our opinion, specific diagnostic criteria for Menetrier's disease should be established first in order to facilitate future studies and establish guidelines

for treatment.

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