

Vikneswaran Namasivayam

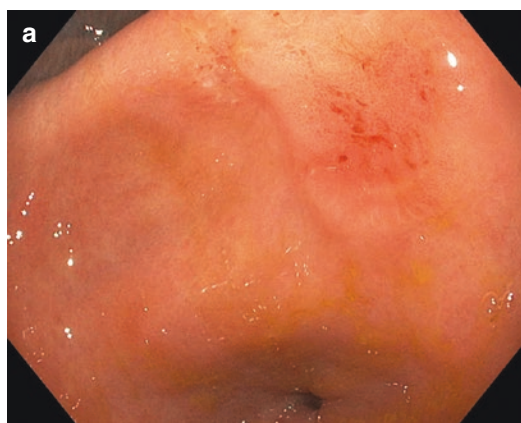
## 19.1 Case 1

An 80-year-old male was referred for further management of a gastric lesion diagnosed on evaluation of iron deficiency anemia. Physical examination was unremarkable. OGD showed a 0IIa lesion at the antrum lesser curve extending to the incisura with two focal ulceration seen raising possibility of deeper invasion. ESD was performed and histology showed gastric adenocarcinoma with superficial submucosal invasion that was within the expanded criteria.

**Diagnosis:** Gastric adenocarcinoma with superficial submucosal invasion within expanded criteria.

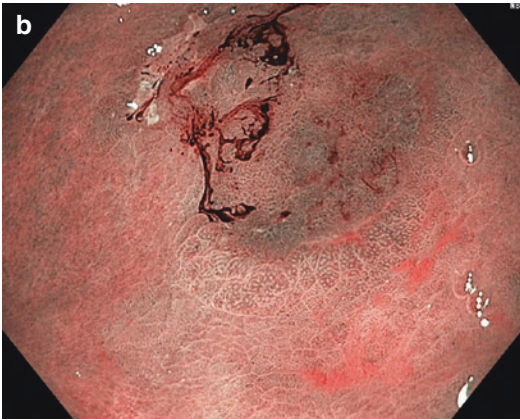
**Discussion:** The presence of early gastric cancer is first suspected on WLE by the presence of an irregular color or surface pattern. The NBI diagnosis of early gastric cancer is made based

on the presence of a demarcation line in combination with irregular microsurface or microvascular pattern [1, 2]. This patient has a lesion in the antrum lesser curve that extends to the incisura. It is characterized by a red mucosa with subtle elevation and central depression. This is readily appreciated when compared to the surrounding gastric mucosa. NBI reveals the presence of a demarcation line as well as abnormal microsurface pattern and loss of microvascular pattern which is consistent with early gastric cancer. Surveillance OGD following ESD reveals mucosal healing on WLE and NBI.

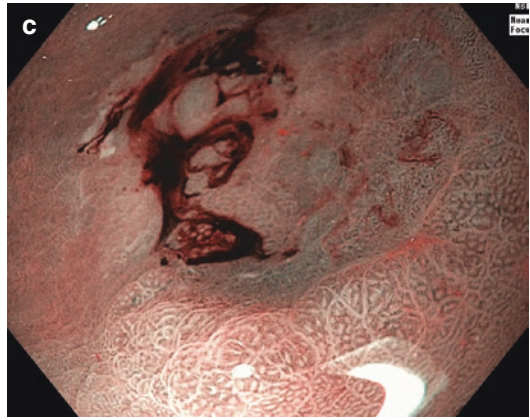


**Fig. 19.1a** WLE of gastric lesion

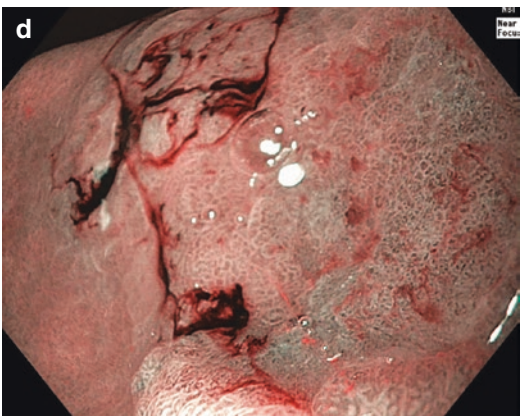
V. Namasivayam (✉)  
Department of Gastroenterology and Hepatology,  
Singapore General Hospital, Singapore, Singapore  
Duke NUS Medical School, Singapore, Singapore  
Yong Loo Lin School of Medicine, Singapore,  
Singapore  
e-mail: [vikneswaran.namasivayam@singhealth.com.sg](mailto:vikneswaran.namasivayam@singhealth.com.sg)



**Fig. 19.1b** NBI view



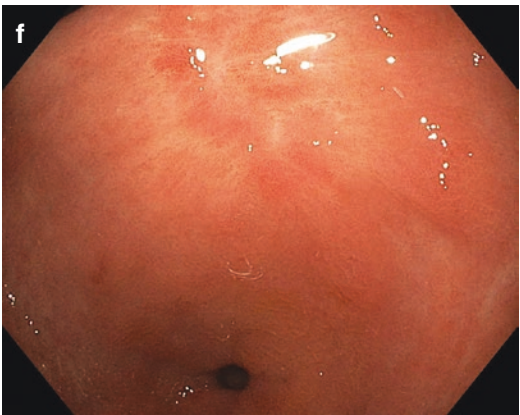
**Fig. 19.1c** NBI with zoom



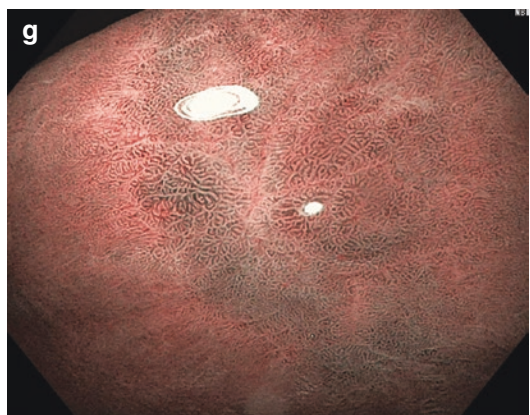
**Fig. 19.1d** NBI with zoom



**Fig. 19.1e** NBI with zoom



**Fig. 19.1f** WLE view of surveillance endoscopy after ESD



**Fig. 19.1g** NBI view of surveillance endoscopy after ESD

## 19.2 Case 2

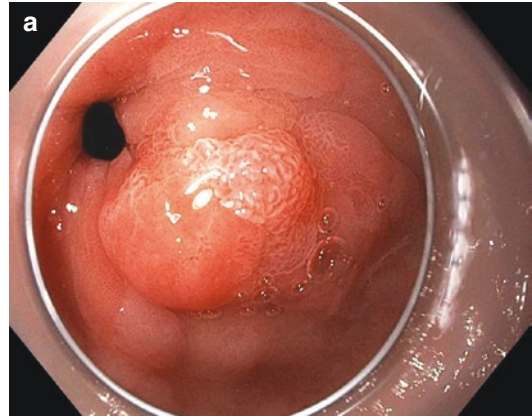
A 77-year-old female was referred for further management of a gastric lesion diagnosed on evaluation of pernicious anemia. Physical examination was unremarkable. OGD showed a 2 cm prepyloric 0IIa lesion extending to the pyloric ring but not involving the duodenum. NBI imaging revealed white opaque substance (WOS) and relatively regular microsurface pattern in remaining mucosa. Platelet count was 83,000.

ESD was performed. Histology of resected specimen was gastric high-grade dysplasia in background of intestinal metaplasia.

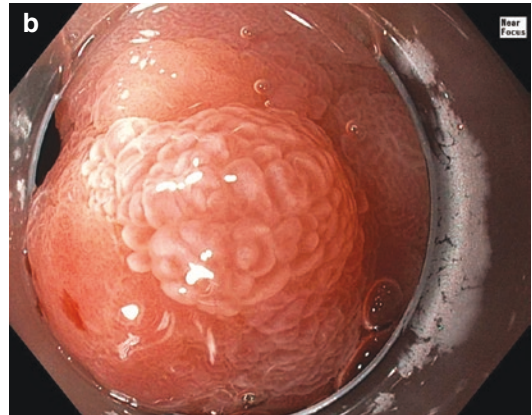
Diagnosis: Gastric prepyloric high-grade dysplasia

Discussion: Pernicious anemia is associated with an increased risk of gastric carcinoma and gastric carcinoid tumors [3]. Magnification endoscopy enables assessment of the microsurface (MS) pattern of the gastric mucosa. NBI with magnification enables assessment of the mucosal microvasculature (MV), which is composed of the subepithelial capillary network (SECN) and collecting venules (CVs). However, in 0IIa gastric lesions the MV pattern may be obscured by WOS [4]. This is evident in this patient who has a WOS deposits with an irregular distribution. WOS correlates with lipid deposits seen on histological specimens after oil red O staining [5]. WOS may be seen in gastric adenoma and carcinoma though more recent studies have described their presence in gastric

intestinal metaplasia as well [6]. The presence and distribution of WOS sign may be used as an adjunctive feature in differentiating adenoma (regular, in line with SECN) from carcinoma (irregular) [4].

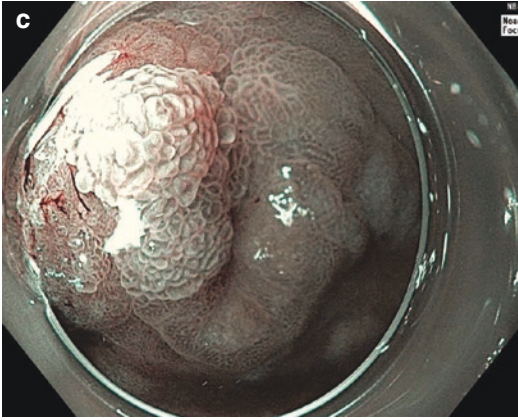


**Fig. 19.2a** Prepyloric lesion demonstrating WOS pattern on WLE

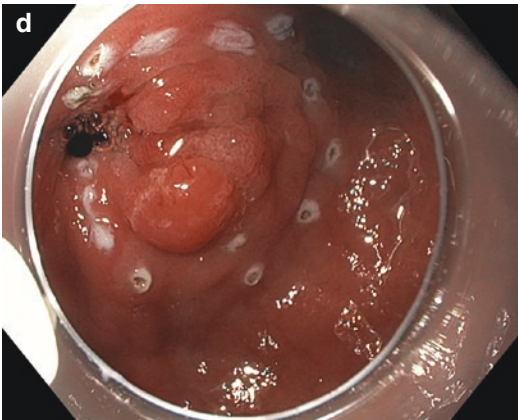


**Fig. 19.2b** WOS pattern seen on WLE with zoom magnification

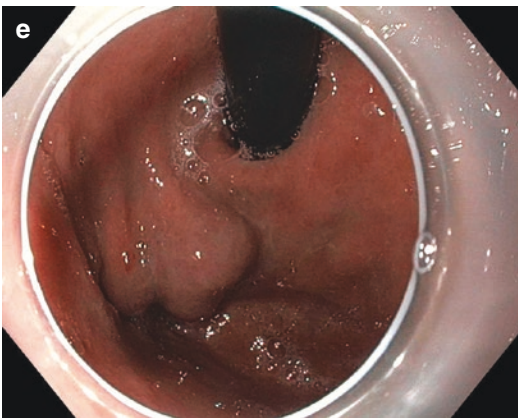




**Fig. 19.2c** WOS pattern seen on NBI with zoom magnification



**Fig. 19.2d** Demarcation of margins for ESD



**Fig. 19.2e** Gastric varix

### 19.3 Case 3

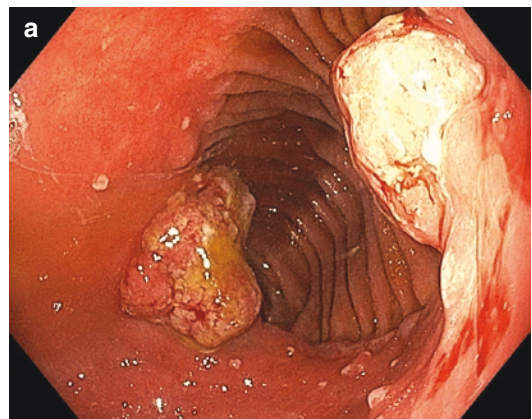
A 67-year-old male underwent OGD for severe iron and vitamin B12 deficiency anemia (Hb 3.4 g/dL). He had a partial gastrectomy with gastrojejunostomy for peptic ulcer bleeding 40 years ago.

OGD showed two gastric nodules (OIs) in the remnant stomach close to the anastomosis. Endoscopic mucosal resection was performed for both nodules. Histology for both nodules revealed intramucosal adenocarcinoma in a hyperplastic polyp.

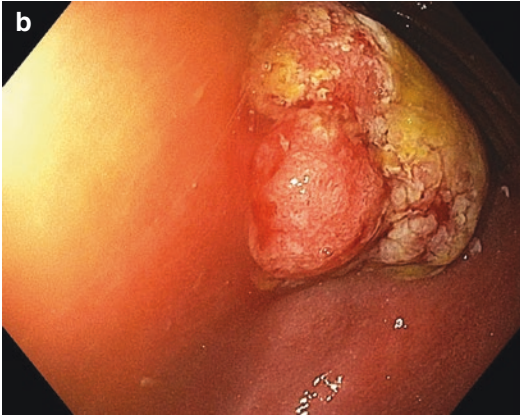
**Diagnosis:** Intramucosal adenocarcinoma in hyperplastic polyps in remnant stomach

**Discussion:** Gastric carcinoma may develop in the remnant stomach several decades after distal gastrectomy for benign disease [7]. Malignant transformation in gastric hyperplastic polyps is uncommon but is more likely in large polyps more than 2 cm. The presence of malignant transformation may be identified on magnifying NBI by changes in the fine mucosal structures (FMS). A reduction in the FMS (known as micrification) compared to the surrounding reference FMS is indicative of the presence of neoplasia in hyperplastic polyps [8].

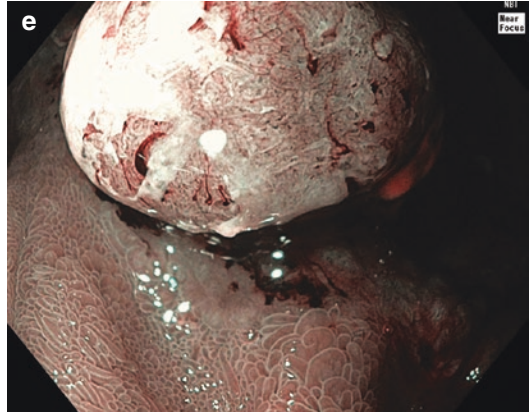
ESD in early gastric cancer in the remnant stomach is technically challenging with higher complication rates due to the limited space for manipulation and the presence of staples and severe fibrosis along the anastomosis and suture line. The rate of perforation for ESD is higher in the remnant stomach especially at the anastomotic site [9, 10].



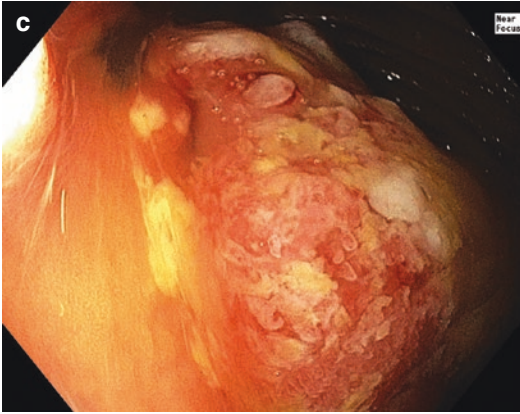
**Fig. 19.3a** Gastric polyps in remnant stomach



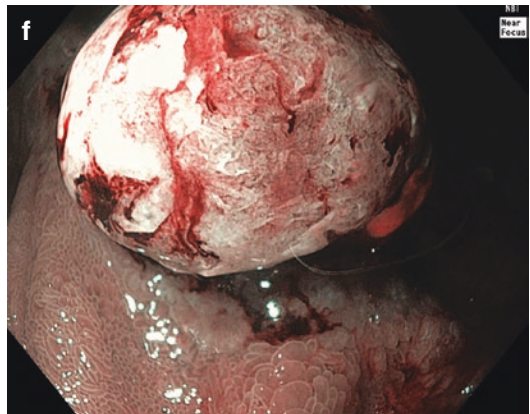
**Fig. 19.3b** Close up view



**Fig. 19.3e** Retroflexed view with NBI zoom



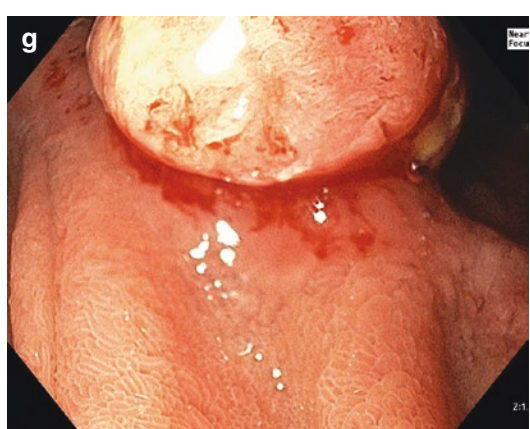
**Fig. 19.3c** Close up view



**Fig. 19.3f** Retroflexed view with NBI zoom

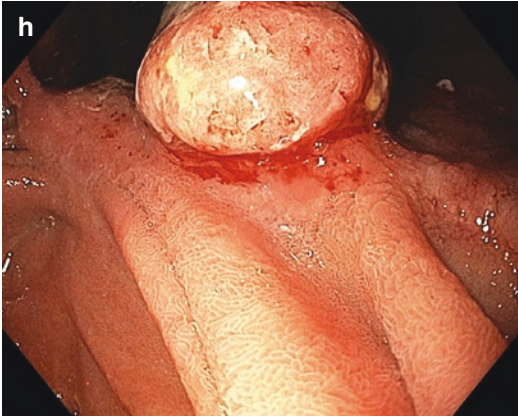


**Fig. 19.3d** Retroflexed view with WLE

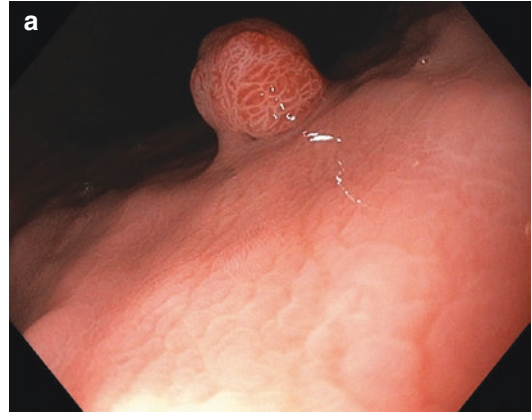


**Fig. 19.3g** Retroflexed view with WLE zoom

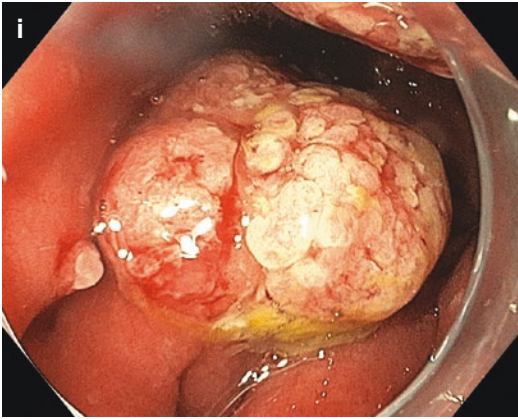




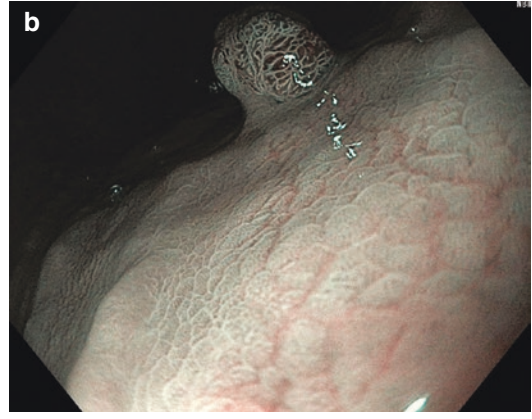
**Fig. 19.3h** Retroflexed view with WLE



**Fig. 19.4a** WLE gastric polyp



**Fig. 19.3i** Close up view



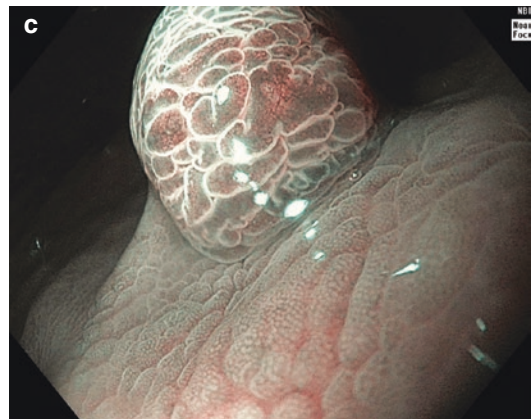
**Fig. 19.4b** NBI gastric polyp

## 19.4 Case 4

A 75-year-old female underwent OGD for unexplained weight loss. It showed a sessile polyp in the gastric body that was resected. Histology was consistent with a gastric hyperplastic polyp.

Diagnosis: Gastric hyperplastic polyp

Discussion: WLE examination reveals a red polypoid lesion with a smooth surface. NBI examination reveals that this polyp has a regular MV and MS (villous) pattern [11]. Malignant transformation is uncommon in gastric hyperplastic polyps. In this patient, there is no evidence of any white opaque substance or micrification within the polyp. This is consistent with the benign histology and absence of malignant transformation [8].



**Fig. 19.4c** NBI with zoom gastric polyp

## 19.5 Case 5

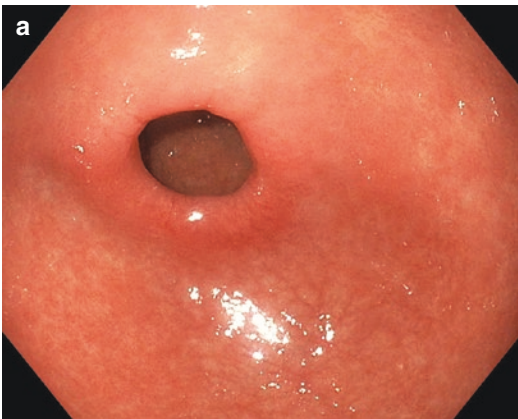
A 56-year-old female underwent gastroscopy for iron and vitamin B12 deficiency anemia. Her intrinsic factor antibody was positive. OGD showed gastric atrophy which was clearly evident even on white light endoscopy.

**Diagnosis:** Pernicious anemia with gastric atrophy

**Discussion:** Pernicious anemia and gastric atrophy are associated with an increased risk of gastric carcinoma [3, 12]. Careful examination on white light endoscopy is crucial as the recognition of gastric atrophy, would prompt a more careful survey for the possible presence of early gastric cancers.

While gastric atrophy is a histological diagnosis, its presence may be predicted by endoscopic features [13]. These would include mucosal discoloration, prominent submucosal vascular pattern due to mucosal thinning, uneven surfaces, and disappearance of folds.

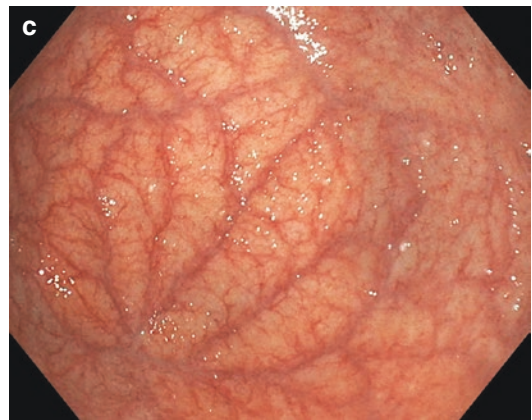
In this patient, the mucosal thinning exposes the underlying submucosal vascular pattern. NBI with optical zoom further characterizes the marked atrophy in the gastric mucosa. The collecting venules are very prominent but the honeycomb-like subepithelial capillary network pattern can hardly be identified. Neither marginal crypt epithelium nor crypt opening can be identified in the atrophic mucosa. These findings are consistent with gastric atrophy.



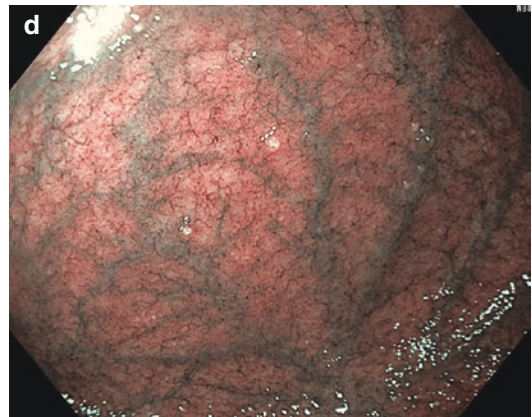
**Fig. 19.5a** WLE gastric atrophy at antrum



**Fig. 19.5b** WLE gastric atrophy at fundus

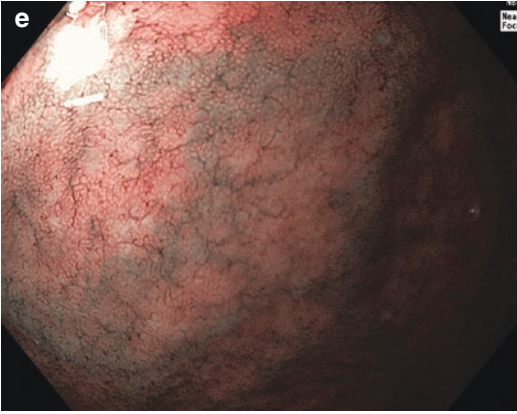


**Fig. 19.5c** WLE gastric atrophy at fundus close-up view

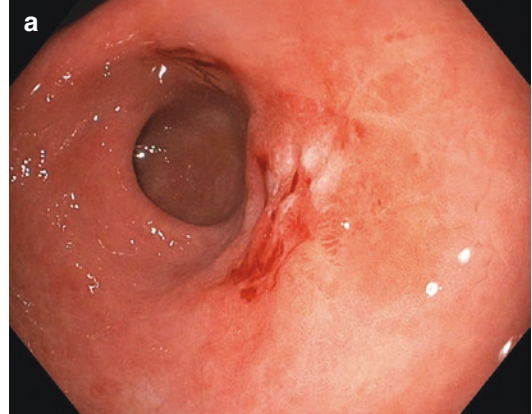


**Fig. 19.5d** NBI gastric atrophy





**Fig. 19.5e** NBI with zoom gastric atrophy



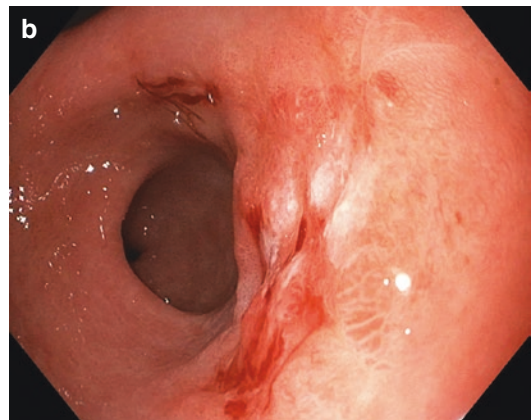
**Fig. 19.6a** WLE gastric lesion

## 19.6 Case 6

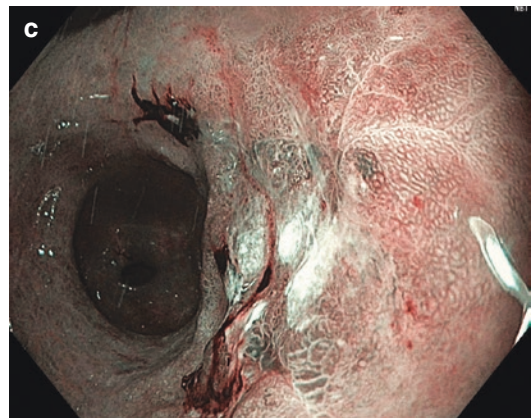
An 81-year-old female was referred for further evaluation of intermittent epigastric pain. A diagnostic OGD was performed. OGD showed a 0IIa lesion with ulceration extending across the posterior wall of the body to the antrum and incisura.

Diagnosis: Gastric cancer

Discussion: The presence of early gastric cancer may be suspected on WLE by the presence of an irregular color or surface pattern. The diagnosis of early gastric cancer may be made on NBI by the presence of a demarcation line in combination with irregular microsurface and microvascular pattern [1, 2]. This patient has a lesion in the posterior wall of the gastric body which is different in color to the surrounding mucosa and demonstrates superficial elevation. NBI evaluation reveals the presence of a demarcation line and loss of microvascular pattern which, once recognized on NBI, may also be appreciated on WLE as well.

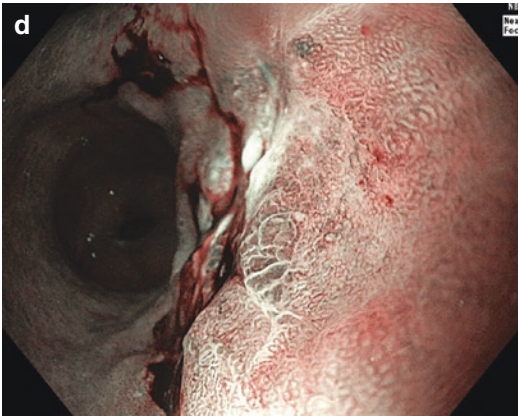


**Fig. 19.6b** WLE close-up view of gastric lesion

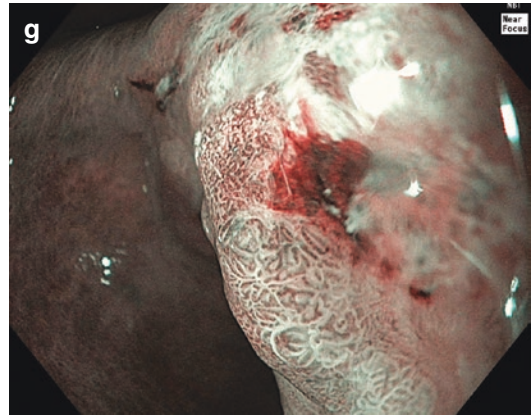


**Fig. 19.6c** NBI close-up view of gastric lesion

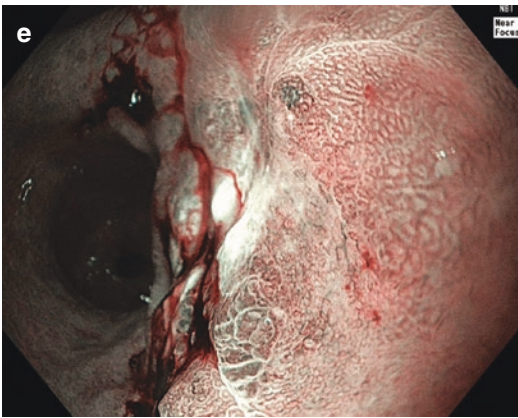




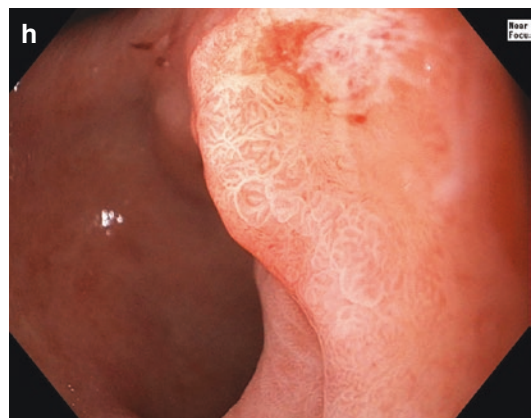
**Fig. 19.6d** NBI with zoom view of demarcation line and IMVP



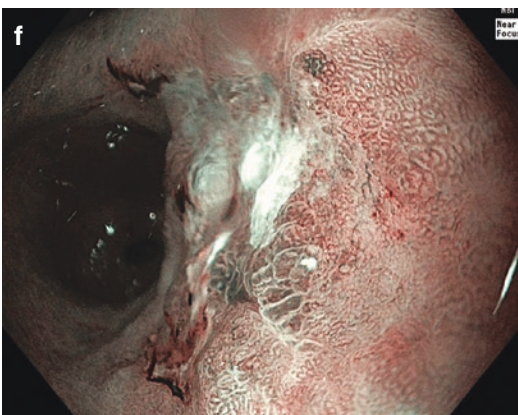
**Fig. 19.6g** NBI with zoom



**Fig. 19.6e** NBI with zoom view of demarcation line and IMVP



**Fig. 19.6h** Corresponding area in WLE with zoom



**Fig. 19.6f** NBI with zoom view of demarcation line and IMVP

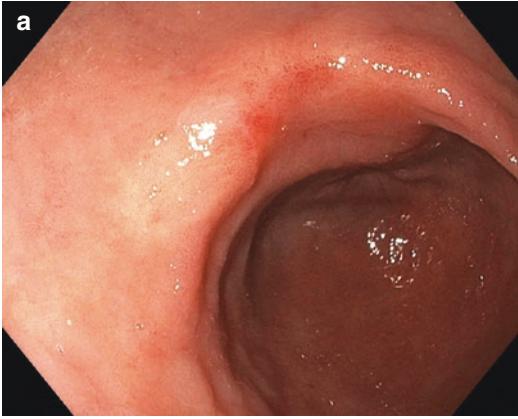
## 19.7 Case 7

A 72-year-old patient underwent OGD for abdominal pain. A previous OGD performed in another country had revealed a *H. pylori* gastric ulcer which had been treated with eradication therapy.

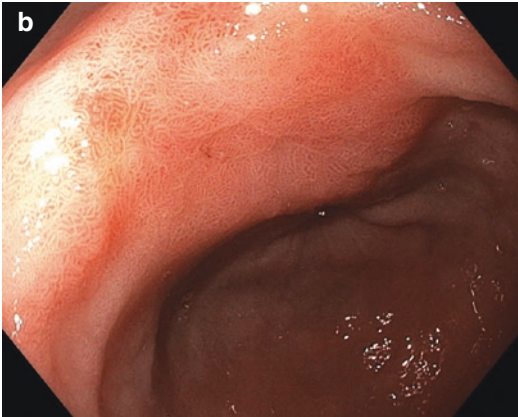
**Diagnosis:** Healed gastric ulcer with intestinal metaplasia

**Discussion:** The identification of a gastric ulcer on OGD raises the possibility of a benign peptic ulcer, malignant ulcer or peptic change within an early gastric cancer. Hence, careful examination is needed to clarify the findings as biopsies may not always be representative. In this

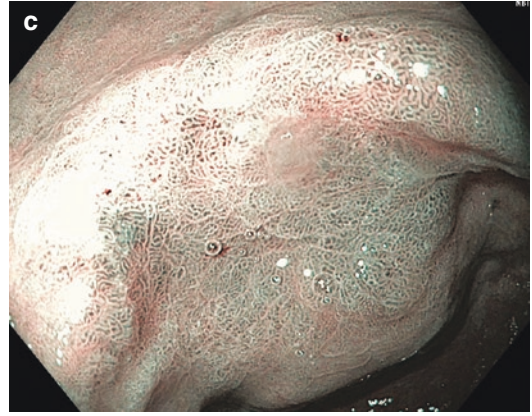
patient, WLE examination reveals abnormal red mucosa in the incisura at the site of the previous gastric ulcer which raises concerns of a sinister diagnosis. However, NBI examination reveals a regular MS, MV pattern and there is no demarcation line. These findings are consistent with gastritis rather than cancer. In addition, light blue crests are seen indicating the presence of intestinal metaplasia.



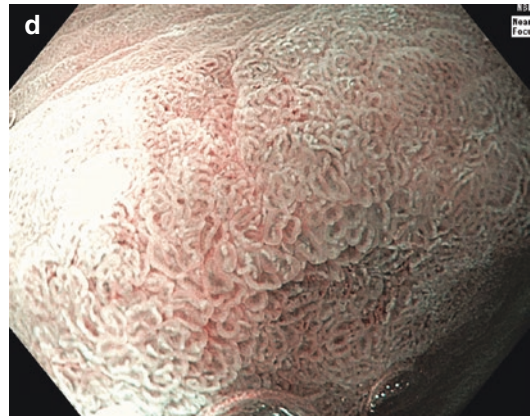
**Fig. 19.7a** WLE of incisura



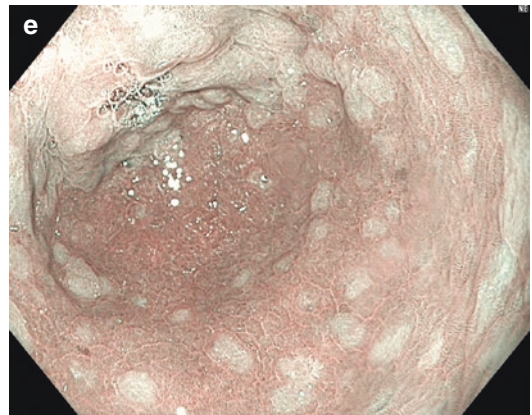
**Fig. 19.7b** WLE close up view of incisura



**Fig. 19.7c** NBI view of incisura



**Fig. 19.7d** NBI with zoom view of incisura showing light blue crests



**Fig. 19.7e** NBI view of antrum

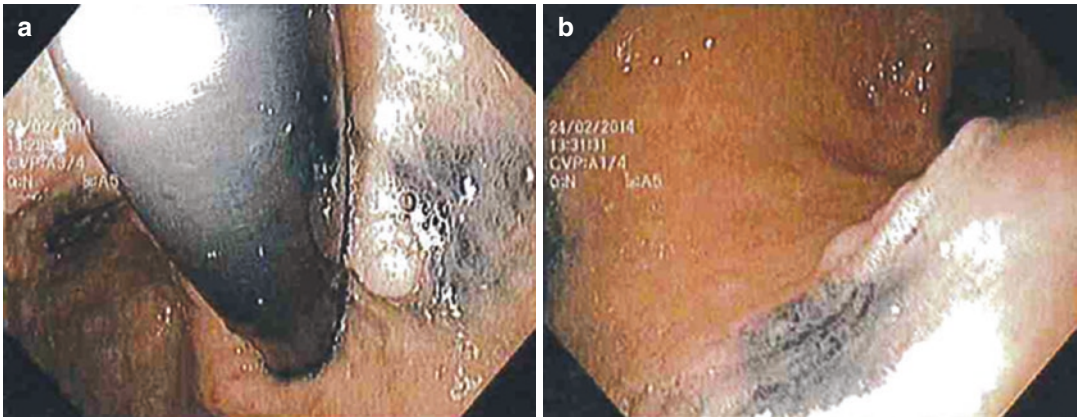


## 19.8 Case 8

A 77-year-old male was referred for further management of a gastric lesion in the proximal stomach that was diagnosed on endoscopic surveillance for gastric intestinal metaplasia. Biopsies showed gastric low-grade dysplasia. Repeat endoscopy in our unit revealed the presence of a 0IIc lesion in the proximal stomach. Unfortunately the lesion had been tattooed which obscured the borders of the lesion and the MS and MV pattern on NBI. Furthermore, the lesion could not be raised, and hence, endoscopic resection could not be performed.

Diagnosis: Tattoo precludes definitive characterization

Discussion: Extensive biopsies, partial endoscopic removal, and tattooing of lesions that are otherwise amenable to endoscopic resection should be avoided [14]. These maneuvers lead to submucosal fibrosis which makes subsequent ESD technically challenging while increasing the risk of perforation during ESD [15]. The presence of fibrosis is indicated by poor lifting after submucosal injection [16]. The need for tattooing can largely be avoided with adequate photo-documentation of the lesion. Endoscopic tattooing, if needed to guide subsequent surgery, should be placed away from the lesion.



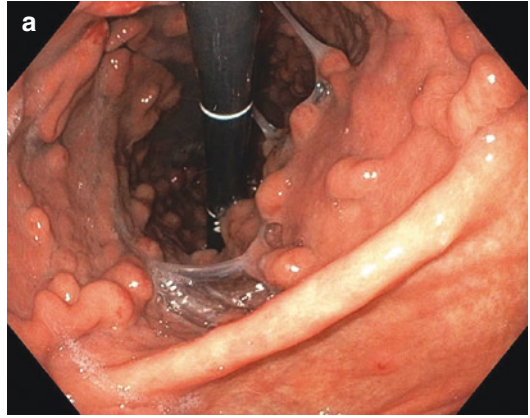
**Fig. 19.8** (a and b) Lesion with tattoo

## 19.9 Case 9

A 63-year-old female presented with vomiting, weight loss, leg edema, and serum hypoalbuminemia (serum albumin 20 g/L). She was referred for further evaluation of suspected linitis plastica on index endoscopy. OGD showed markedly thickened gastric mucosal folds with adherent mucoid secretion (gastric pH 7) primarily affecting the proximal stomach with relative sparing of the antrum.

Diagnosis: Menetrier's Disease

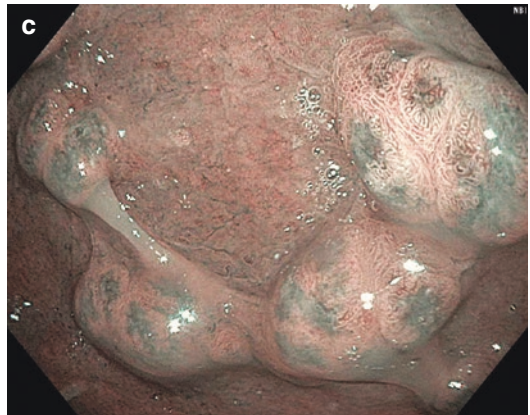
Discussion: Menetrier's Disease is a rare protein-losing gastropathy characterized by hyperproliferative gastric foveolar epithelium. It is caused by dysregulated epidermal growth factor receptor signaling that leads to expansion of surface mucous cells in the body and fundus of the stomach [17]. The presenting symptoms include epigastric pain, vomiting, generalized edema, and hypoalbuminemia [18]. Endoscopy demonstrates enlargement of gastric folds which is usually confined to the oxyntic mucosa (body and fundus). Sparing of the antrum is typical but not invariable [19]. Diagnosis is confirmed by biopsies showing marked foveolar hyperplasia and glandular atrophy and a paucity of inflammatory infiltrates. The demonstration of glandular atrophy may require full-thickness mucosal biopsies. The differential diagnoses would include polyps and polyposis syndromes. These are differentiated from Menetrier's Disease by family history, extra-gastric manifestations, genetic testing, endoscopic appearance, and histological presentation. Juvenile polyposis syndrome (JPS) patients may have colonic polyps or a family history of JPS. Cronkhite–Canada syndrome may have characteristic hyperpigmentation, hair and nail changes in addition to multiple hamartomatous polyps throughout the gastrointestinal tract [19]. Other differential diagnoses to consider would include lymphoma, gastric carcinoma, gastrointestinal stromal tumors (GIST), tuberculosis, or other infiltrative disease [17]. CMV associated forms of Menetrier's Disease have been described [20, 21]. Cetuximab, a monoclonal antibody to the epidermal growth factor receptor, has been reported to be an effective treatment for Menetrier's Disease [22]. There have also been reports of remission with *H. pylori* eradication.



**Fig. 19.9a** Prominent folds in proximal stomach with mucoid secretions



**Fig. 19.9b** Antrum is relatively normal



**Fig. 19.9c** Appearance on NBI



## References

1. Yao K. The endoscopic diagnosis of early gastric cancer. *Ann Gastroenterol*. 2013;26(1):11–22.
2. Ezoe Y, Muto M, Uedo N, Doyama H, Yao K, Oda I, et al. Magnifying narrowband imaging is more accurate than conventional white-light imaging in diagnosis of gastric mucosal cancer. *Gastroenterology*. 2011;141(6):2017–25. e3
3. Murphy G, Dawsey SM, Engels EA, Ricker W, Parsons R, Etemadi A, et al. Cancer Risk After Pernicious Anemia in the US Elderly Population. *Clin Gastroenterol Hepatol*. 2015;13(13):2282–9 e1–4.
4. Yao K, Iwashita A, Tanabe H, Nishimata N, Nagahama T, Maki S, et al. White opaque substance within superficial elevated gastric neoplasia as visualized by magnification endoscopy with narrow-band imaging: a new optical sign for differentiating between adenoma and carcinoma. *Gastrointest Endosc*. 2008 Sep;68(3):574–80.
5. Yao K, Iwashita A, Nambu M, Tanabe H, Nagahama T, Maki S, et al. Nature of white opaque substance in gastric epithelial neoplasia as visualized by magnifying endoscopy with narrow-band imaging. *Dig Endosc*. 2012 Nov;24(6):419–25.
6. Kanemitsu T, Yao K, Nagahama T, Imamura K, Fujiwara S, Ueki T, et al. Extending magnifying NBI diagnosis of intestinal metaplasia in the stomach: the white opaque substance marker. *Endoscopy*. 2017 Jun;49(6):529–35.
7. Shimada H, Fukagawa T, Haga Y, Oba K. Does remnant gastric cancer really differ from primary gastric cancer? A systematic review of the literature by the Task Force of Japanese Gastric Cancer Association. *Gastric Cancer*. 2016;19(2):339–49.
8. Horiuchi H, Kaise M, Inomata H, Yoshida Y, Kato M, Toyozumi H, et al. Magnifying endoscopy combined with narrow band imaging may help to predict neoplasia coexisting with gastric hyperplastic polyps. *Scand J Gastroenterol*. 2013;48(5):626–32.
9. Takenaka R, Kawahara Y, Okada H, Tsuzuki T, Yagi S, Kato J, et al. Endoscopic submucosal dissection for cancers of the remnant stomach after distal gastrectomy. *Gastrointest Endosc*. 2008;67(2):359–63.
10. Tanaka S, Toyonaga T, Morita Y, Fujita T, Yoshizaki T, Kawara F, et al. Endoscopic submucosal dissection for early gastric cancer in anastomosis site after distal gastrectomy. *Gastric Cancer*. 2014;17(2):371–6.
11. Omori T, Kamiya Y, Tahara T, Shibata T, Nakamura M, Yonemura J, et al. Correlation between magnifying narrow band imaging and histopathology in gastric protruding/or polypoid lesions: a pilot feasibility trial. *BMC Gastroenterol*. 2012;12:17.
12. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, et al. Helicobacter pylori infection and the development of gastric cancer. *N Engl J Med*. 2001;345(11):784–9.
13. Kono S, Gotoda T, Yoshida S, Oda I, Kondo H, Gatta L, et al. Can endoscopic atrophy predict histological atrophy? Historical study in United Kingdom and Japan. *World J Gastroenterol*. 2015;21(46):13113–23.
14. Kim HG, Thosani N, Banerjee S, Chen A, Friedland S. Effect of prior biopsy sampling, tattoo placement, and snare sampling on endoscopic resection of large nonpedunculated colorectal lesions. *Gastrointest Endosc*. 2015;81(1):204–13.
15. Kim JH, Nam HS, Choi CW, Kang DH, Kim HW, Park SB, et al. Risk factors associated with difficult gastric endoscopic submucosal dissection: predicting difficult ESD. *Surg Endosc*. 2017;31(4):1617–26.
16. Takeuchi Y, Iishi H, Tanaka S, Saito Y, Ikematsu H, Kudo SE, et al. Factors associated with technical difficulties and adverse events of colorectal endoscopic submucosal dissection: retrospective exploratory factor analysis of a multicenter prospective cohort. *Int J Color Dis*. 2014;29(10):1275–84.
17. Coffey RJ, Washington MK, Corless CL, Heinrich MC. Menetrier disease and gastrointestinal stromal tumors: hyperproliferative disorders of the stomach. *J Clin Invest*. 2007;117(1):70–80.
18. Meuwissen SG, Ridwan BU, Hasper HJ, Innemee G. Hypertrophic protein-losing gastropathy. A retrospective analysis of 40 cases in The Netherlands. The Dutch Menetrier Study Group. *Scand J Gastroenterol Suppl*. 1992;194:1–7.
19. Rich A, Toro TZ, Tanksley J, Fiske WH, Lind CD, Ayers GD, et al. Distinguishing Menetrier's disease from its mimics. *Gut*. 2010;59(12):1617–24.
20. Setakhr V, Muller G, Hoang P, Lambert AS, Geubel A. Cytomegalovirus-associated protein losing gastropathy in an immunocompetent adult: a case report. *Acta Gastro-Enterol Belg*. 2007;70(3):296–9.
21. Drut RM, Gomez MA, Lojo MM, Drut R. Cytomegalovirus-associated Menetrier's disease in adults. Demonstration by polymerase chain reaction (PCR). *Medicina*. 1995;55(6):659–64.
22. Fiske WH, Tanksley J, Nam KT, Goldenring JR, Slebos RJ, Liebler DC, et al. Efficacy of cetuximab in the treatment of Menetrier's disease. *Sci Transl Med*. 2009;1(8):8ra18.