Gastric Lymphomas and Other Gastric Malignancies

13

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13.1 Gastric Lymphomas

13.1.1 Definition

Gastric lymphomas manifest either primary gastric lymphoma or gastric metastasis of systemic lymphoma. Primary gastric lymphoma is defined by that the tumor presents extranodal localization and, after routine staging procedures, constitutes the predominant disease localization in the stomach. It accounts for 1–5% of all primary gastric malignancies. Tumor stage as well as histologic subtype is the most important prognostic factor.

13.1.2 Staging Systems

The Ann Arbor stage and TNM classification (Table 13.1) were proposed to describe the depth of tumor invasion, extent of nodal involvement, and local tissue infiltration by lymphoma [1].

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Table 13.1 Staging systems for gastrointestinal lymphomas

Modified Ann Arbor system	Paris staging system	Spreading of lymphomas
I1E	T1N0M0	Mucosa, submucosa
I2E	T2N0M0	Muscularis propria, subserosa
I2E	T3N0M0	Serosa penetration
I2E	T4N0M0	Per continuitatem infiltration of neighboring organs
II1E	T1-4N1M0	Regional lymph nodes (compartment I + II)
II2E	T1-4N2M0	Intra-abdominal distant lymph nodes
IIIE	T1-4N3M0	Extra-abdominal lymph nodes
IV	T1-4N0-3M1	Diffuse or disseminated infiltration of distant or extra-gastrointestinal organs
	B1	Bone marrow

13.1.3 Endoscopy

Endoscopic features of gastric lymphomas can be categorized into three different types: (1) exophytic with polypoid masses, (2) ulcero-infiltrative, and (3) hypertrophic with large, nodular folds (Fig. 13.1). However, at times, the features are nonspecific with mucosal hyperemia, edema, friability, or erosions. Gastric lymphomas should be differentiated from other gastric diseases including gastric carcinoma, rugal hypertrophic gastritis, acute gastric mucosal lesions, or NSAID-induced gastritis.

Deep biopsies are often required because gastric lymphomas arise from subepithelial lymphoid tissue. In addition, tumor samples should be obtained sufficiently for an accurate histologic subtyping of lymphomas by specific molecular or genetic markers.

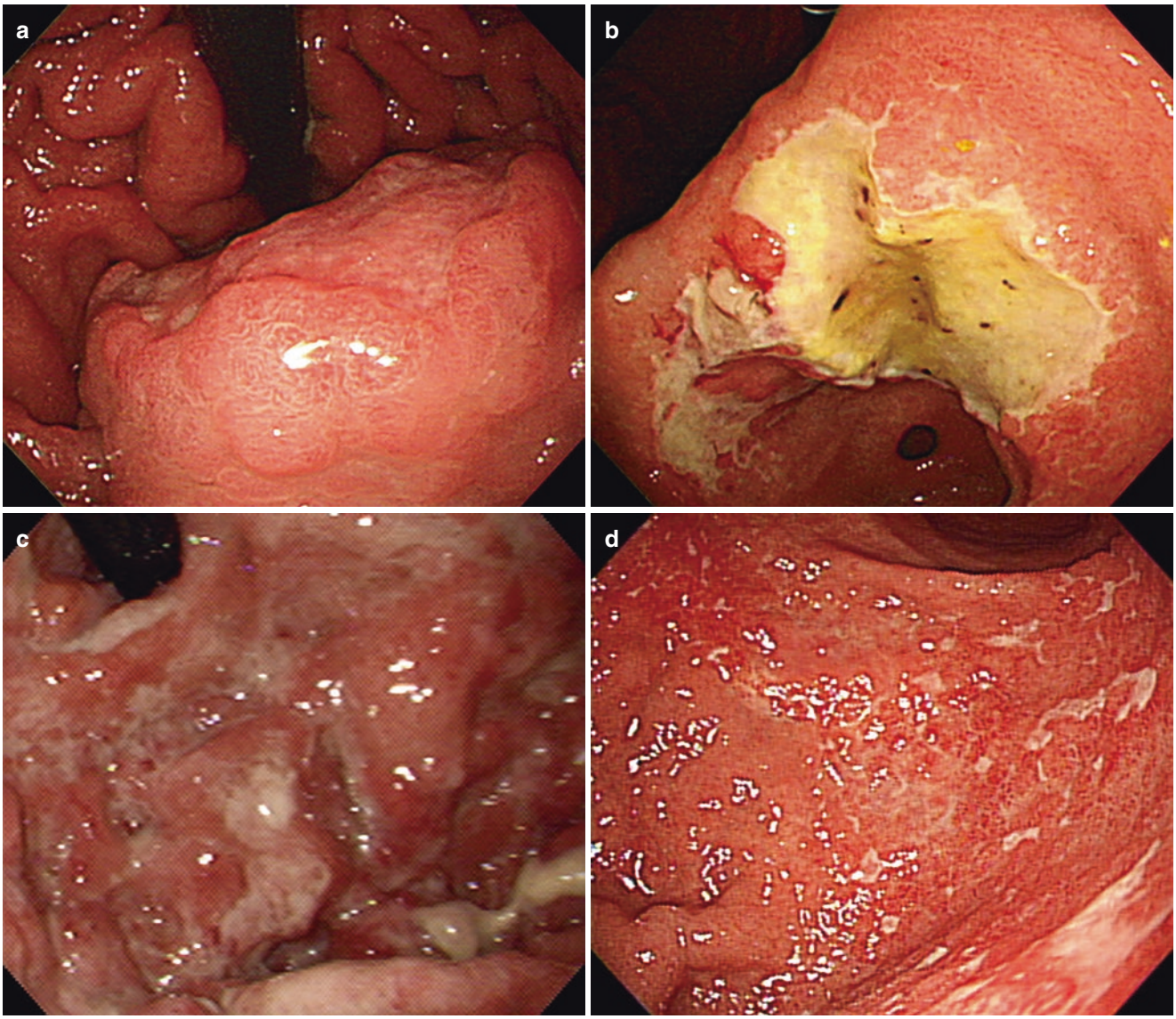

Fig. 13.1 Endoscopic features of gastric lymphomas. (**a**) exophytic mass, (**b**) ulcerative infiltration, (**c**) hypertrophic thick folds, (**d**) ill-defined hyperemia and erosions

13.1.4 Histological Subtypes

13.1.4.1 Gastric Extranodal Marginal Zone B-Cell Lymphoma of MALT

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissues (MALT) is a B-cell non-Hodgkin lymphoma with perifollicular, marginal zone growth of small lymphocytes. MALT lymphoma is the most common type of gastric lymphomas. *Helicobacter pylori* (*H. pylori*) is the main causative agent, and more than 90% of cases are associated with the infection.

Endoscopic findings of gastric MALT lymphoma vary from minimal mucosal changes to ulceration or masses mimicking gastric carcinoma (Fig. 13.2). Because there is no unique appearance indicating MALT lymphoma, endoscopic biopsy should be taken in any suspicious lesions.

Stage is the most important prognostic factor of gastric MALT lymphoma. Endosonography is the only technique that visualizes the layers of the gastric wall. It enables to define depth of tumor invasion (T1-4) and metastasis to regional lymph nodes (N0-1).

H. pylori eradication is highly effective in treating gastric MALT lymphomas [2]. Tumors confined to the mucosa or submucosa (I1E) regress more frequently than that with deeper invasion. *H. pylori* eradication is not successful in regression of higher stage MALT lymphoma.

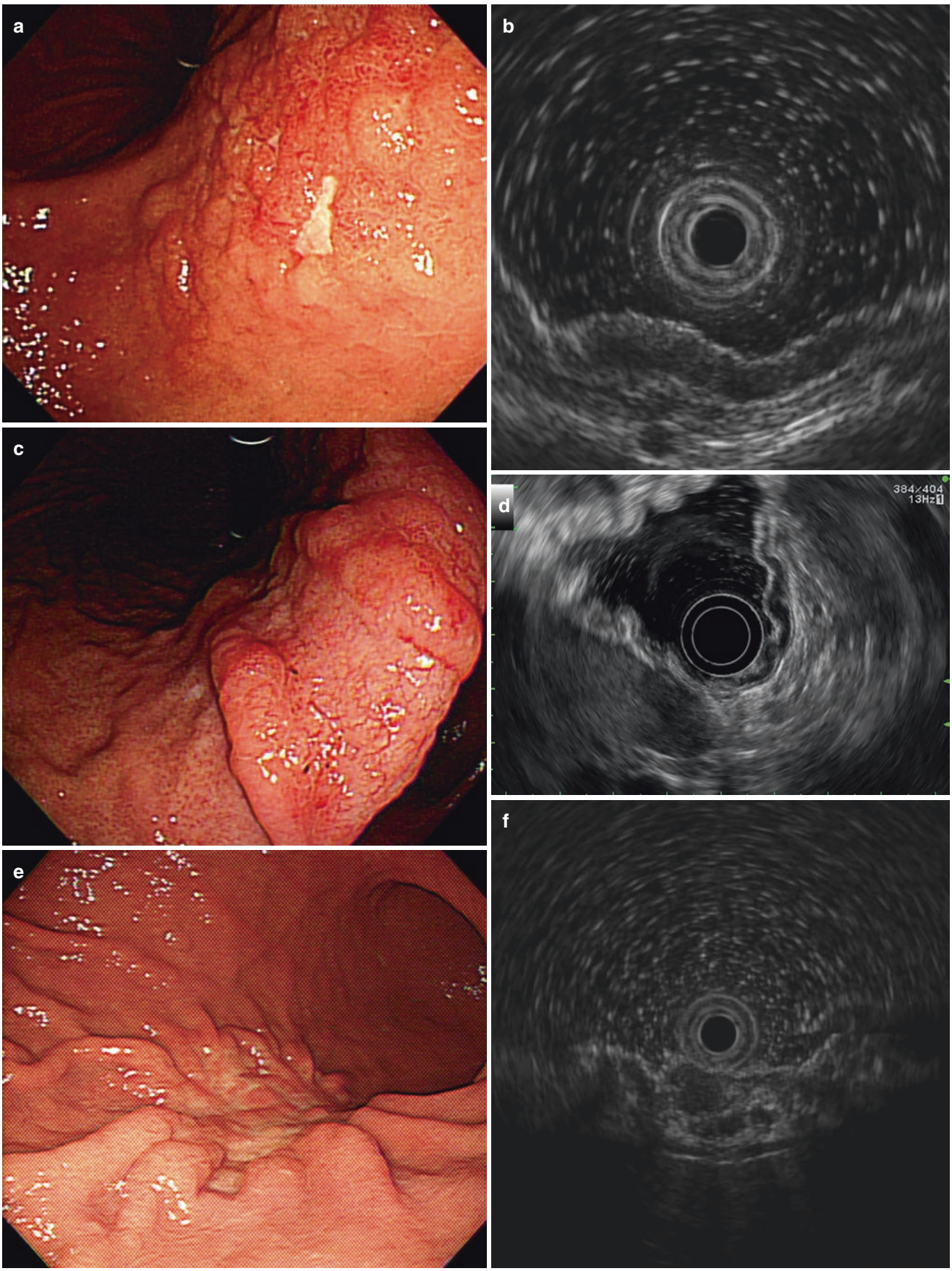

Fig. 13.2 Gastric MALT lymphoma. (**a**) Hyperemic, irregular erosions. (**b**) Hypoechoic thickening of mucosal layer (T1m). (**c**) Rugal hypertrophy. (**d**) Hypoechoic tumoral infiltration in the submucosa (T1sm). (**e**) Ulceration with fold changes. (**f**) Submucosal invasion of tumors (T1sm). (**g**) Ulcerative mass. (**h**) Hypoechoic tumor infiltration in the muscularis propria (T2). (**i**) Diffuse infiltration with friability. (**j**) Irregular outer border of the muscularis propria (T2)

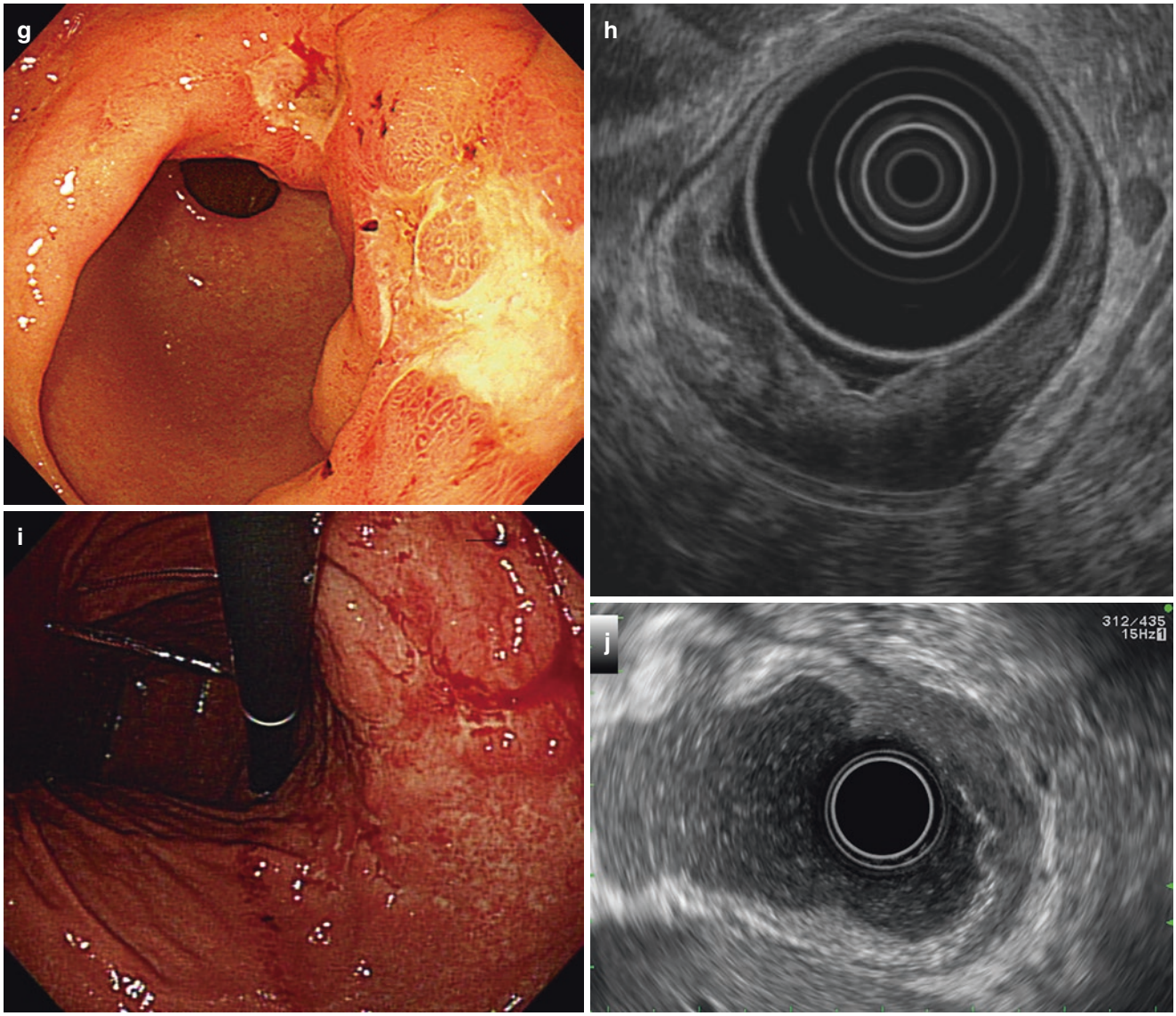

Fig. 13.2 (continued)

13.1.4.2 Diffuse Large B-Cell Lymphoma

Excluding gastric MALT lymphoma, diffuse large B-cell lymphoma (DLBCL) accounts for approximately 60% of all gastric lymphomas. Gastric DLBCL is an aggressive lymphoma that might arise de novo or from MALT lymphoma transformation. Endoscopy features include exophytic mass, ulcerative infiltration, or hypertrophic thick folds (Fig. 13.3).

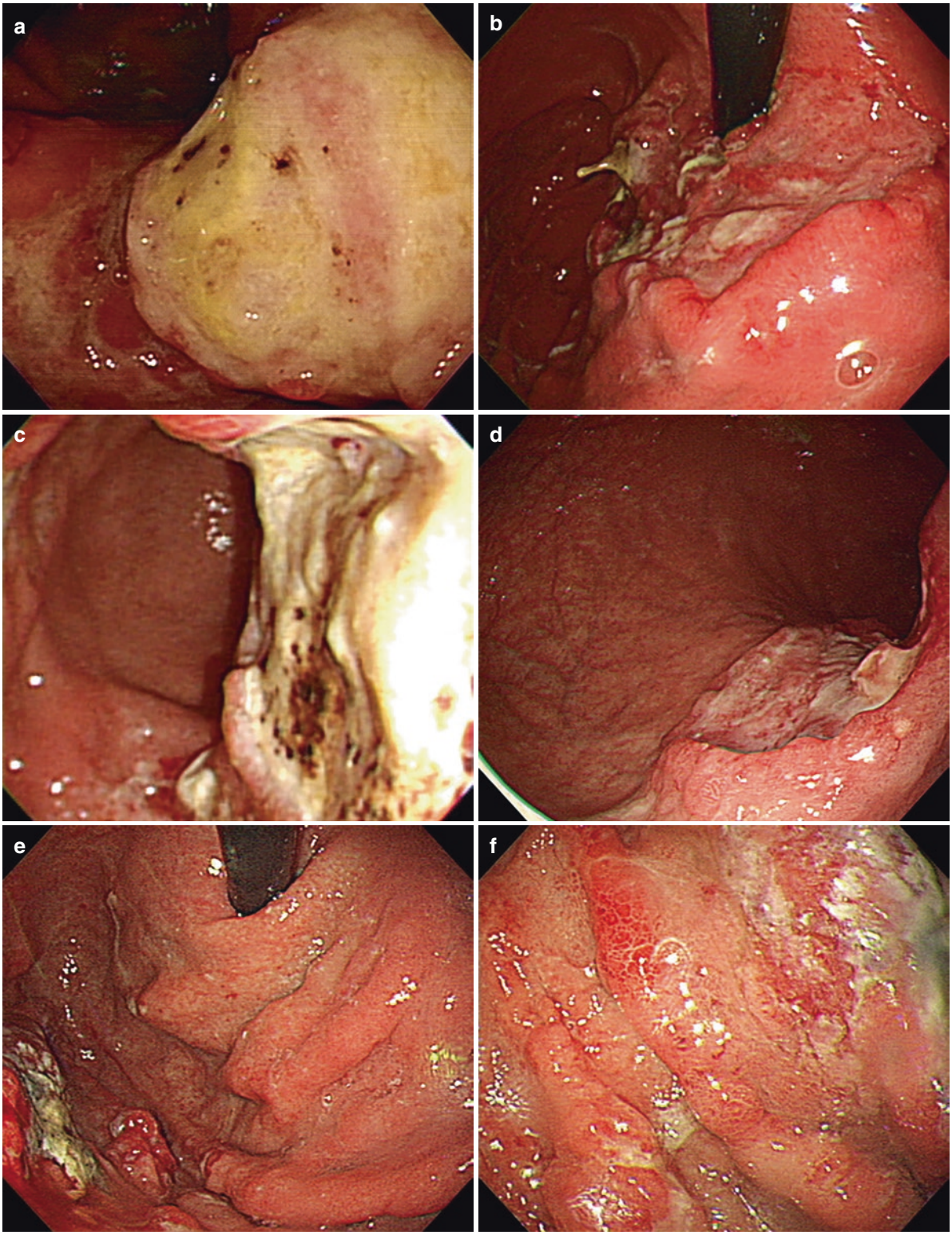

Fig. 13.3 Diffuse large B-cell lymphoma. (**a**) exophytic mass, (**b**–**d**) ulcerative mass, (**e**–**f**) hypertrophic thick folds

13.1.4.3 Mantle Cell Lymphoma

Primary gastrointestinal mantle cell lymphoma is rare with a frequency of 4–9% of all gastrointestinal non-Hodgkin lymphomas. It was first described, so-called, as multiple lymphomatous polyposis (Fig. 13.4). Typically, multiple lymphomatous polyps in various diameters involve several digestive tracts. Some of the lesions are ulcerative.

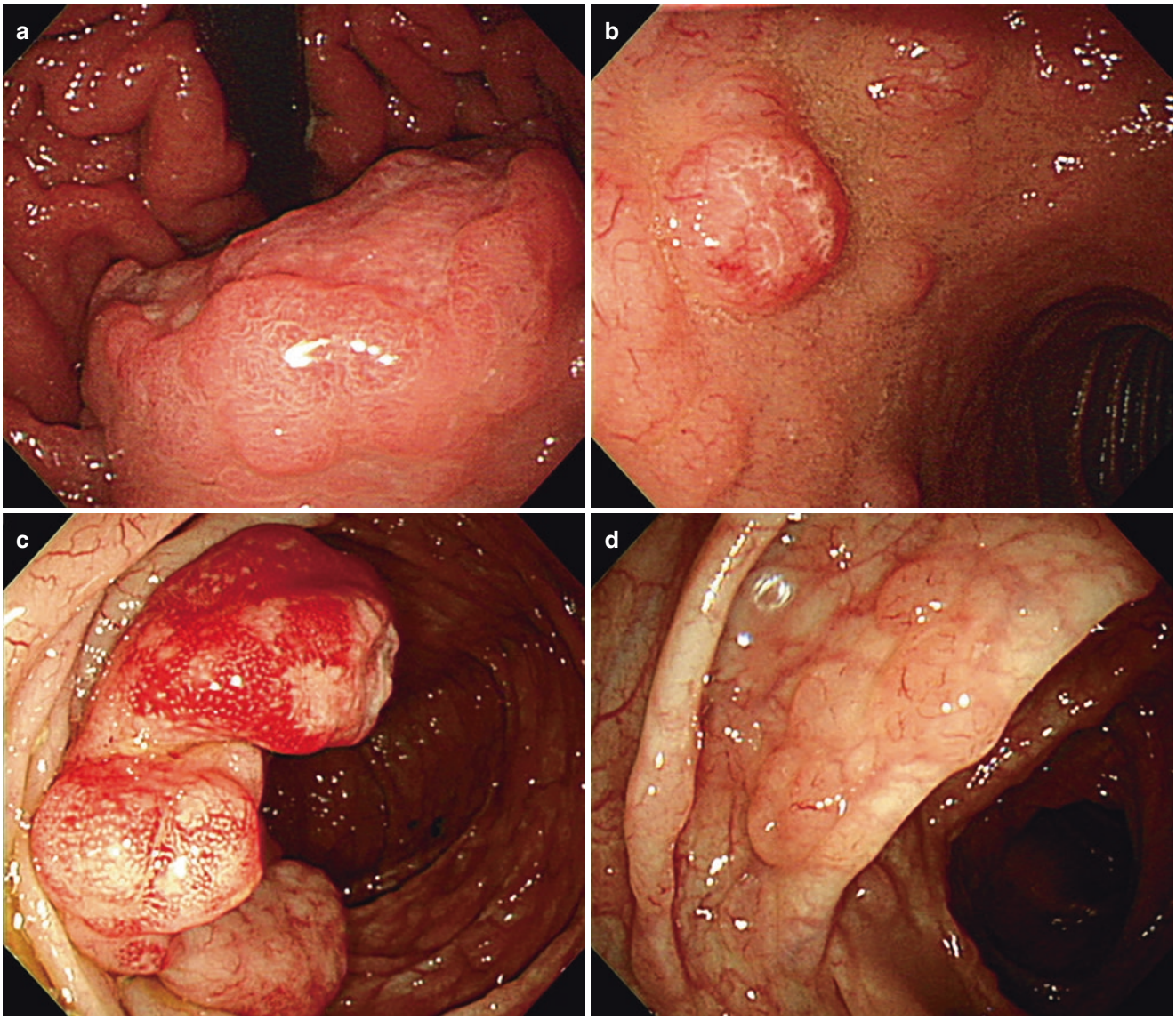

Fig. 13.4 Multiple lymphomatous polyposis of mantle cell lymphoma. (**a**) Ulcerated gastric mass, (**b**) duodenal polyps, (**c**, **d**) colonic mass with numerous small polyps

13.1.4.4 Enteropathy-Type T-Cell Lymphoma

Enteropathy-associated T-cell lymphoma (EATL) is a rare form of aggressive T-cell lymphoma accounting for less than 1% of non-Hodgkin lymphomas. EATL can be divided into two types. Type I is the most common and highly associated with adult-onset celiac disease. This type mostly presents with malabsorption, weight loss, and celiac disease-related symptoms. Type II may occur sporadically and has no association with celiac disease. This type presents often with obstruction or perforation of the small bowel.

Most EATL are localized in the proximal small intestine, particularly in the jejunum. However, the tumors may occur at the ileum, colon, or stomach. When T-cell lymphomas develop in the stomach, they are usually associated with infection by human T-lymphotropic virus type 1.

EATL is often multifocal and may show mucosal flattening or ulceration on endoscopy (Fig. 13.5). Occasionally, the tumor forms an ulcerative mass that invades the intestinal wall. Rarely, EATL present as a bulky mass or as a submucosal tumor.

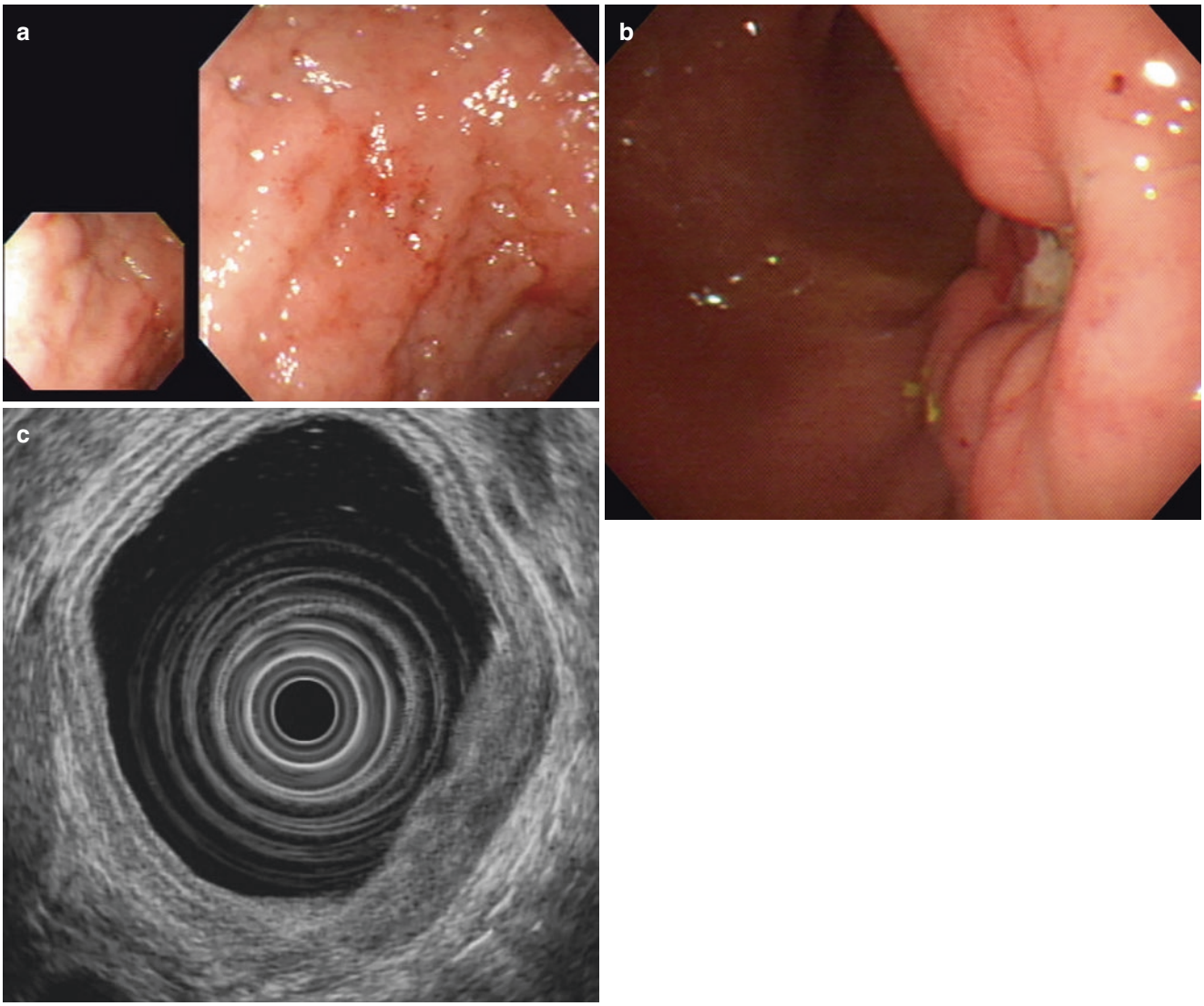

Fig. 13.5 Enteropathy-type T-cell lymphoma. (**a**) Multiple, erosive, and superficial infiltration of enteropathy-associated T-cell lymphoma in the duodenum, (**b**, **c**) ulcerative T-cell lymphoma

13.2 Other Gastric Malignancies

13.2.1 Gastric Neuroendocrine Tumors (Gastric Carcinoids)

13.2.1.1 Definition

Gastrointestinal neuroendocrine tumors (NETs; gastric carcinoids) are categorized into: (1) well-differentiated NETs, (2) well-differentiated neuroendocrine carcinomas, and (3) poorly differentiated neuroendocrine carcinomas. Neuroendocrine carcinomas are defined as the tumors with vascular invasion, invasion into the deeper walls, or with distant metastasis.

13.2.1.2 Clinicopathological Classification

Gastric NETs can be classified into four types based on histologic grade and underlying clinical conditions (Table 13.2) [3]. Histologically, the tumors are graded as G1, G2, or G3 on the basis of proliferative activity (Ki-67 index, mitotic rate).

Table 13.2 Clinicopathological characteristics of neuroendocrine neoplasms of the stomach

	Gastric NETs (gastric carcinoids)			
	Type 1	Type 2	Type 3	Poorly differentiated neuroendocrine gastric cancer (type 4)
Relative frequency	70%–80%	5%–6%	14%–25%	6%–8%
Features	Often small (<10 mm) and multiple	Often small (<10 mm) and multiple	Solitary, often >20 mm	Solitary, often ulcerated >20 mm
Associated conditions	CAG	MEN1/ZES[a]	No	No
Histology[a]	Well-differentiated G1	Well-differentiated G1	Well-differentiated G1/G2	Poorly differentiated, G3
Serum gastrin	Very high or high	Very high or high	Normal	Mostly normal
Gastric pH	Anacidic	Hyperacidic	Normal	Mostly normal
Metastases	<10%	10%–30%	50%–100%	80%–100%
Tumor-related deaths	No	<10%	25%–30%	>>50%

CAG Chronic atrophic gastritis, *MEN1* Multiple endocrine neoplasia type1, *ZES* Zollinger-Ellison syndrome, *NET* neuroendocrine tumor
[a]G1 and G2 indicate a well-differentiated tumor; G3 most often is poorly differentiated (value of Ki-67 index: G1 0%–2%, G2 3%–20%, and G3>20%)

13.2.1.3 Endoscopy

The vast majority of gastric NETs manifests as multifocal, small gastric polyps in the atrophic gastric mucosa (type 1) or as part of Zollinger-Ellison syndrome (type 2) (Fig. 13.6). By contrast, type 3 gastric NETs or poorly differentiated carcinoma (type 4) presents as solitary ulcerative mass. Endosonography is a procedure to visualize tumor size and depth of intramural invasion.

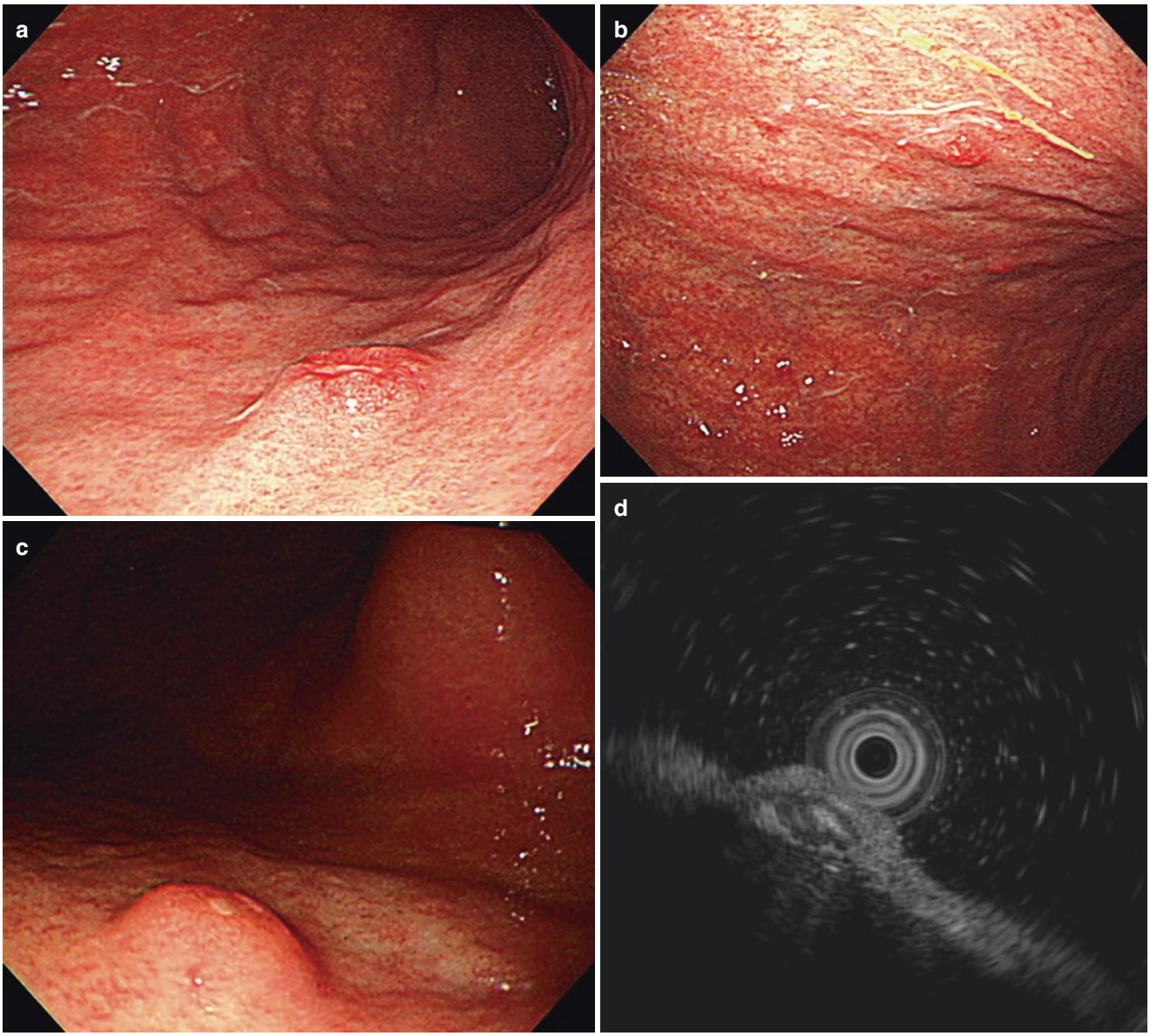

Fig. 13.6 Types of gastric carcinoids. (**a**–**c**) Multifocal small polyps of type 1, (**d**) hypoechoic small tumor within the deep mucosa, (**e**, **f**) type 3 with solitary intramural mass, (**g**) ulcerative mass of type 4, poorly differentiated carcinoma

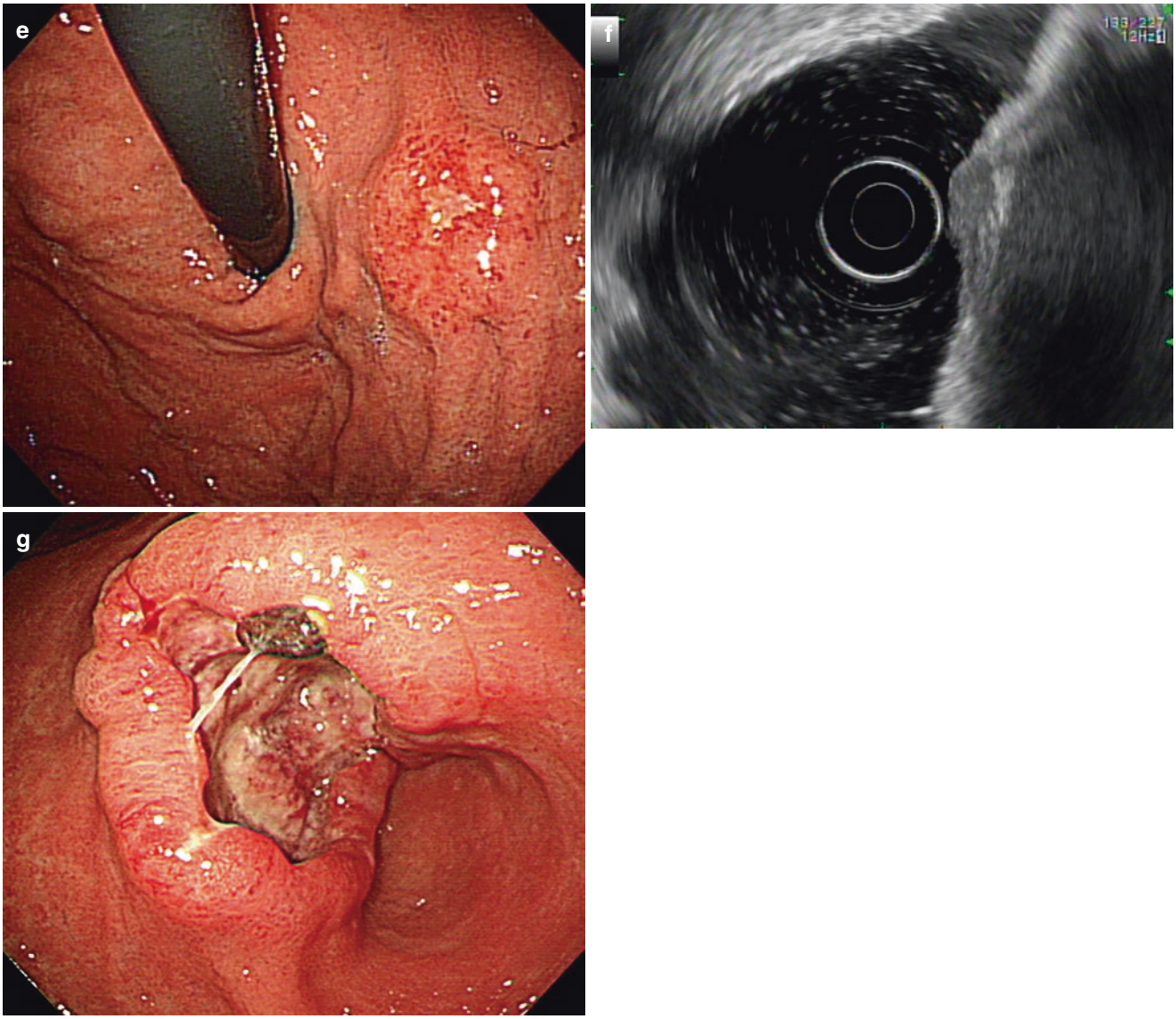

Fig. 13.6 (continued)

13.2.2 Gastric Metastasis from Malignancies of Other Organs

Metastatic tumors to the stomach are rarely found in melanoma and lung and breast cancers [4]. Clinical manifestation includes gastrointestinal bleeding or anemia. Polypoid masses with erosions or ulcerations are common endoscopic features (Fig. 13.7). The metastatic tumors may present multiple lesions located in the upper part of the stomach, which mimic submucosal tumors at times.

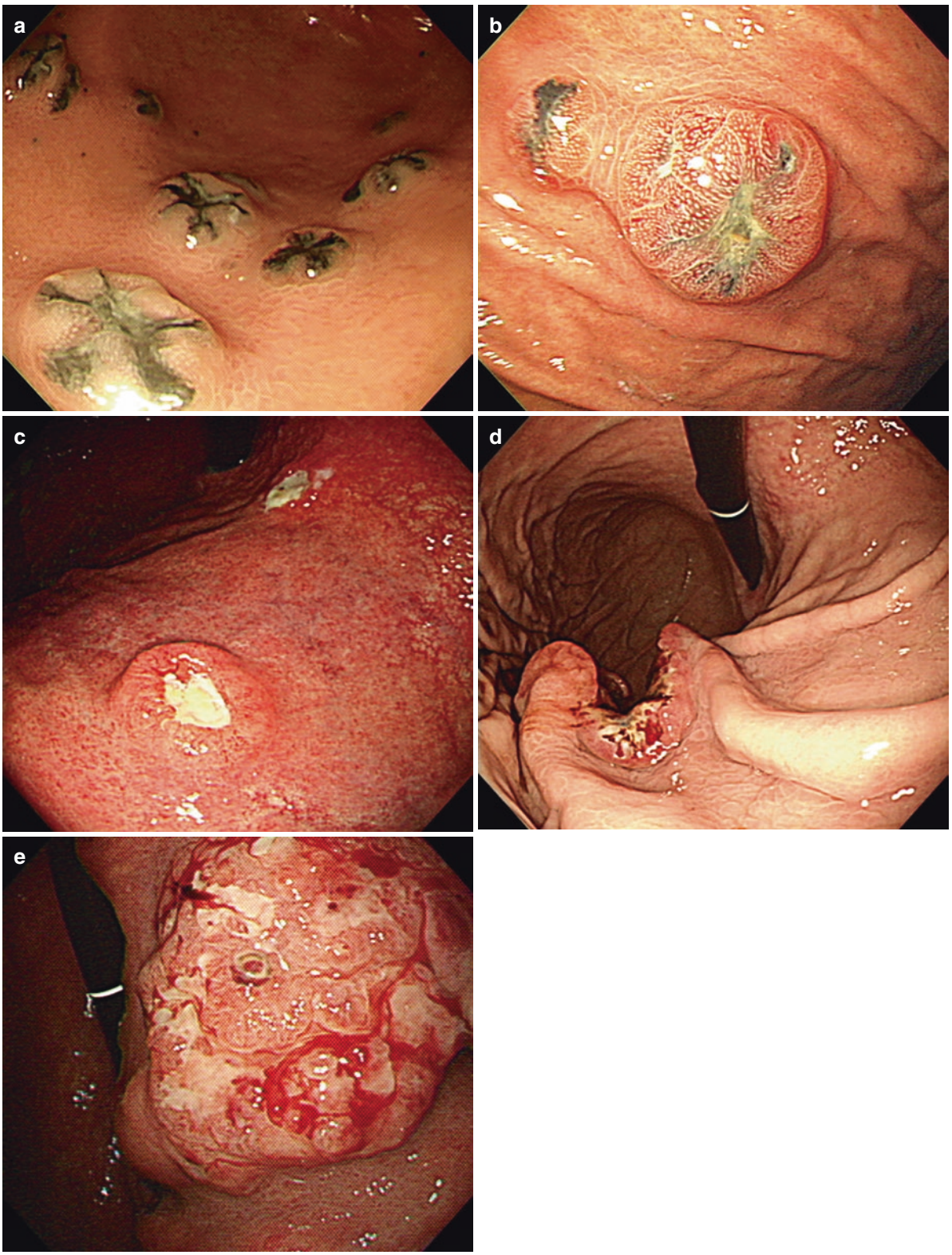

Fig. 13.7 Gastric metastasis. (**a**, **b**) Exophytic masses with dark pigments (melanoma), (**c**) multiple ulceration (lung cancer), (**d**) ulcerofungating mass (lung cancer), (**e**) hemorrhagic mass (hepatocellular carcinoma)

References

1. Ruskoné-Fourmestraux A, Fischbach W, Aleman BM, EGILS group, et al. EGILS consensus report. Gastric extranodal marginal zone B-cell lymphoma of MALT. Gut. 2011;60:747–58.
2. Zullo A, Hassan C, Cristofari F, et al. Effects of *Helicobacter pylori* eradication on early stage gastric mucosa-associated lymphoid tissue lymphoma. Clin Gastroenterol Hepatol. 2010;l8:105–10.
3. Scherübl H, Cadiot G, Jensen RT, et al. Neuroendocrine tumors of the stomach (gastric carcinoids) are on the rise: small tumors, small problems? Endoscopy. 2010;42:664–71.
4. Oda, Kondo H, Yamao T, et al. Metastatic tumors to the stomach: analysis of 54 patients diagnosed at endoscopy and 347 autopsy cases. Endoscopy. 2001;33:507–10.