Infectious and Noninfectious Esophagitis

3

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In addition to gastroesophageal reflux which is the most common cause of esophagitis, there are so various etiologic factors which can cause esophageal injury (Table 3.1). In immunocompromised patients, infectious esophagitis due to virus and fungi is frequently developed. Although pathologic review is necessary to confirm the diagnosis of viral esophagitis, endoscopic examination is very useful to diagnose Candida esophagitis where multiple white mucosal plaquelike lesions are typical. Esophagitis can develop because of various noninfectious causes such as trauma, chemical injury, and radiation. In these cases, precise history taking in addition to endoscopic findings is important. In pill-induced esophagitis, symmetrical kissing-type ulcers are frequent. Esophagitis also can be presented as a kind of clinical manifestation of other systemic or skin diseases. In this chapter, endoscopic findings of various types of esophagitis except reflux esophagitis will be discussed with examples.

Table 3.1 Classification of nonreflux esophagitis

Infectious esophagitis
Viral
Herpes
Cytomegalovirus
Fungal
Candida
Bacterial
Noninfectious esophagitis
Pill-induced
Contact esophagitis
Corrosive
Radiation
Eosinophilic esophagitis
Behçet's disease associated
Skin disease associated

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3.1 Infectious Esophagitis

Esophageal infection occurs predominantly in immunocompromised hosts resulting from immunosuppressive treatment or infection with human immunodeficiency virus (HIV), although involvement of healthy individuals can infrequently occur. Other causative microorganisms in infectious esophagitis include Candida, cytomegalovirus (CMV), herpes simplex virus (HSV), and some bacteria [1].

3.1.1 Viral Esophagitis

3.1.1.1 HSV

HSV can infect esophageal mucosa by reactivation via the vagus nerve or direct extension from oropharynx. Most infections are related to HSV type 1, despite several HSV type 2 cases. HSV esophagitis is usually observed in immunocompromised patients but can occasionally be found in immunocompetent individuals. Endoscopy with histopathological examination is necessary to confirm the diagnosis of HSV esophagitis. The earliest manifestation is a vesicle usually involving the distal esophagus, although this early stage can be rarely seen on endoscopy. The usual finding is the presence of multiple small shallow ulcers formed by coalescence of preceding vesicles (Fig. 3.1). The ulcers are usually well demarcated, and the intervening mucosa appears normal. Other findings that can be present include exudates, plaques, or diffuse erosions. Biopsies or brushing for histopathological examination should be taken from the edge of the ulcers because viral cytopathic effects are most likely to be present there.

3.1.1.2 CMV

CMV is another genus of the herpes virus family that can establish a latent infection after the resolution of acute infection. Both reactivation of latent CMV and reinfection with a novel exogenous strain can cause clinical problems in the host. Many organ systems, such as the gastrointestinal (GI) tract, liver, neurologic system, and cardiovascular system, can be targets for CMV infection. Esophagitis is the second most common GI manifestation of CMV infection after colitis, and CMV esophagitis may superimpose CMV colitis. It is nearly always observed in immunocompromised patients. To confirm the diagnosis, upper GI endoscopy with pathologic examination is used (Fig. 3.2). In contrast to HSV esophagitis, the ulcers in CMV esophagitis tend to be linear or longitudinal and deeper. However, shallow ulcers or multiple discrete lesions mimicking HSV esophagitis also can be found, especially in the distal esophagus. For the biopsy, sufficient specimens (>10) should be taken from the base of the ulcers because CMV infects the submucosal fibroblasts and vascular endothelium.

3.1.1.3 HIV

HIV can cause esophageal ulcers resembling CMV lesions in esophagitis at time of seroconversion (Fig. 3.3). However, in patients with acquired immunodeficiency syndrome (AIDS), esophagitis with multiple pathogens can be a problem (Fig. 3.4).

3.1.2 Fungal Esophagitis

Although several kinds of fungi including cryptococcus, histoplasma, blastomyces, or aspergillus rarely can cause esophagitis, Candida is the most common fungal cause of esophagitis.

3.1.2.1 Candida Esophagitis

Candida is a multispecies yeast genus. Although most human species are harmless commensals or symbionts, *C. albicans* can infect humans or animals, especially immunocompromised patients. Other risk factors of Candida esophagitis include broad spectrum antibiotics, steroid, diabetes, malnutrition, or long-term acid suppression therapy. While infections may be focally or systemically invasive, the local mucous membranes are usually involved including oropharynx, esophagus, and vulvovagina. The causative organism is almost always *C. albicans*. The diagnosis of choice is upper GI endoscopy with biopsy or brushing. Diffusely distributed multiple white or yellowish mucosal plaquelike lesions are the typical findings in endoscopy (Fig. 3.5). The plaques are easily removable from the mucosa by the endoscope. If pathologic examination shows yeasts and pseudohyphae invading mucosal cells, the diagnosis of Candida esophagitis is confirmed.

3.1.3 Bacterial Esophagitis

Bacterial esophagitis is rare and can be diagnosed when there is histopathologically demonstrable bacterial invasion of esophageal mucosa or deeper layers with no concomitant fungal, viral, or neoplastic involvement or previous surgery of the esophagus. It should be considered as a possible cause in all immunocompromised patients who present with odynophagia. Endoscopy can show various appearances ranging from normal mucosa to ulcers associated with erythema, plaques, pseudomembranes, or hemorrhage. Mucosal biopsy and culture are necessary to confirm the diagnosis.

3.1.3.1 Tuberculous Esophagitis

Although rare in developed countries, GI tuberculosis is not uncommon in developing countries. However, esophageal manifestation is extremely rare. In the esophagus, tuberculosis infection usually occurs in the middle region and shows ulcerative, tumorlike lesions (Fig. 3.6). Since the density of tuberculous granulomas in the infected tissue may be low and tuberculous granulomas are located in the submucosal layer, multiple and deep tissue biopsies are necessary to confirm this diagnosis.

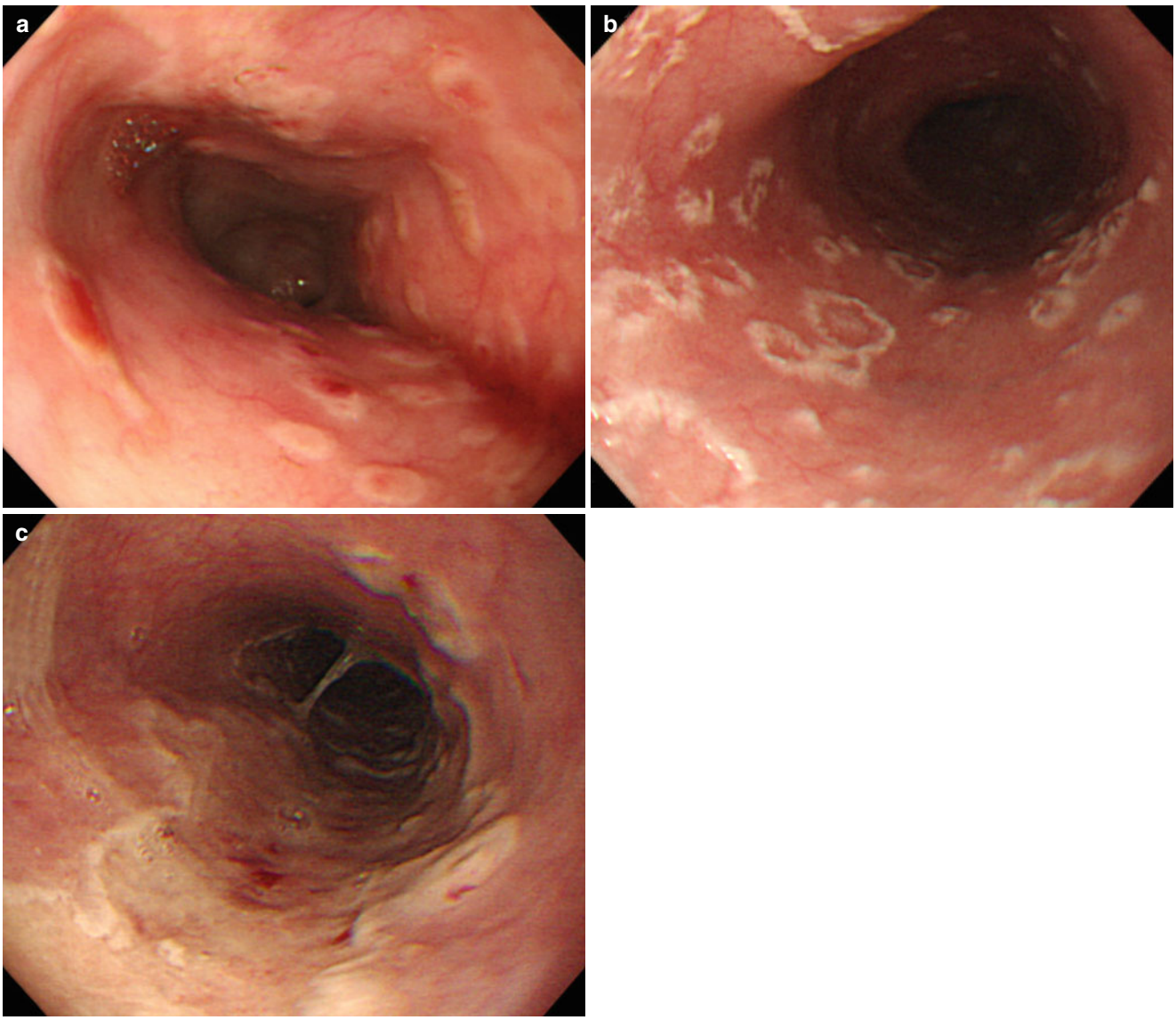

Fig. 3.1 Herpes esophagitis. (**a**) Multiple vesicular lesions, (**b**) shallow ulcers with prominent demarcation, (**c**) large ulcer formation by confluence of small ulcers

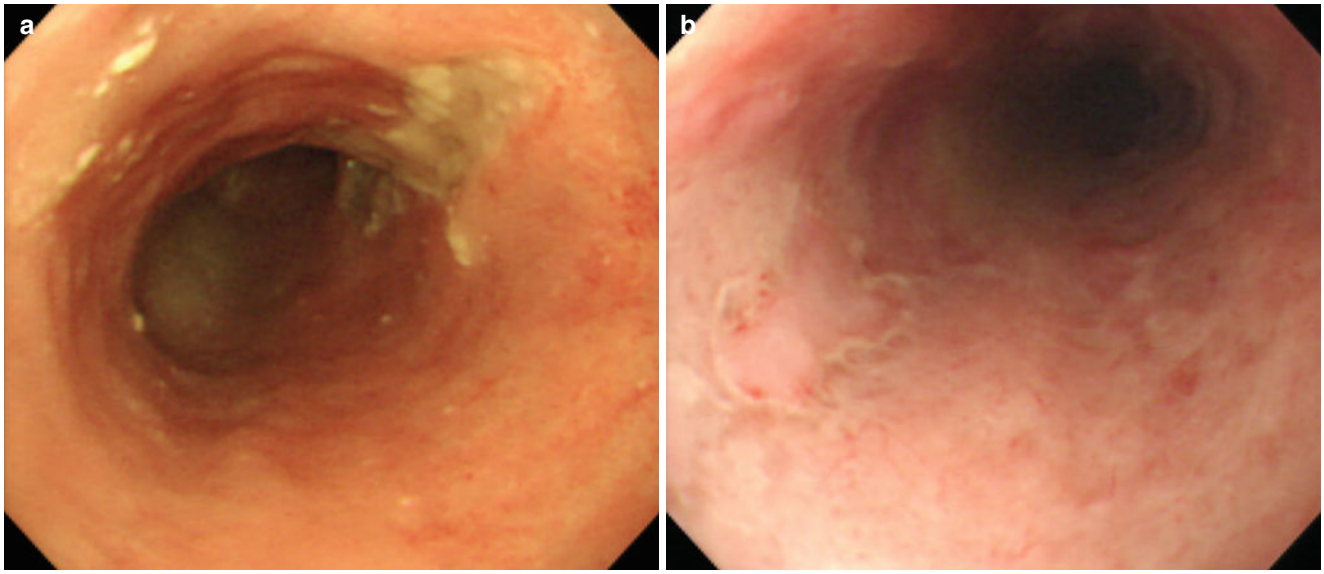

Fig. 3.2 CMV esophagitis. (**a**) Longitudinal deep ulcer, (**b**) multiple shallow ulcers mimicking herpes esophagitis

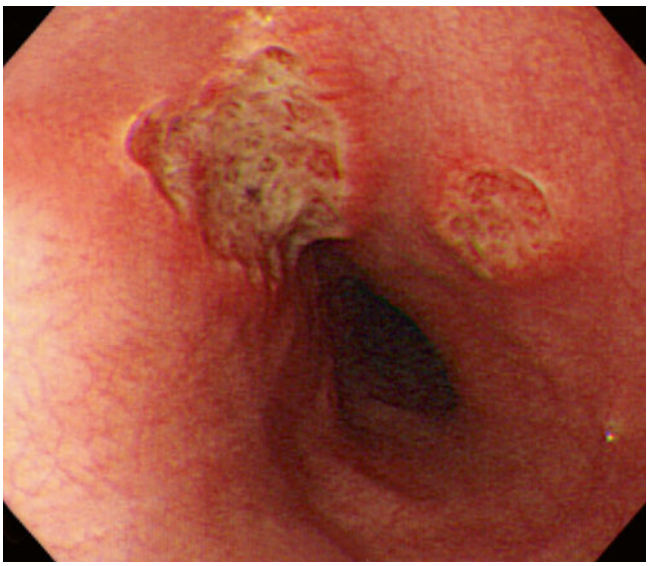

Fig. 3.3 HIV esophagitis. Several well-demarcated ulcers resembling CMV esophagitis can be present in HIV-postive individuals, in the absence of immunohistochemical staining evidence of CMV and HSV

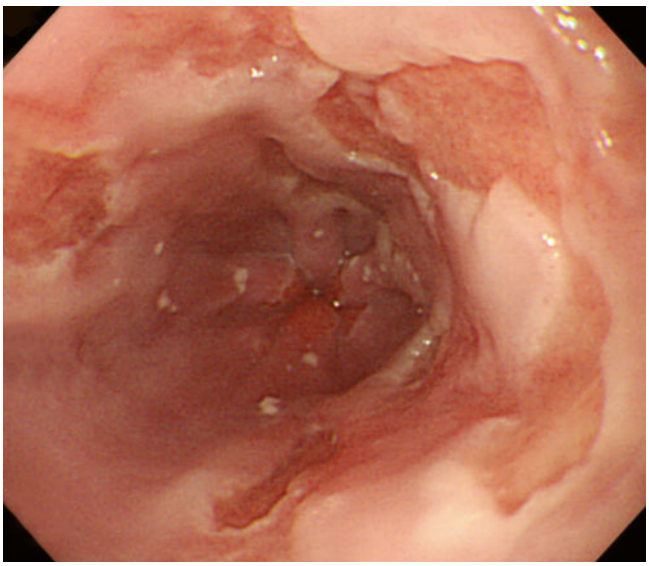

Fig. 3.4 Multi-pathogenic esophagitis in an AIDS patient. Various types of ulcers and white plaques are observed. Candida, HSV, and CMV immunohistochemical stains were all positive

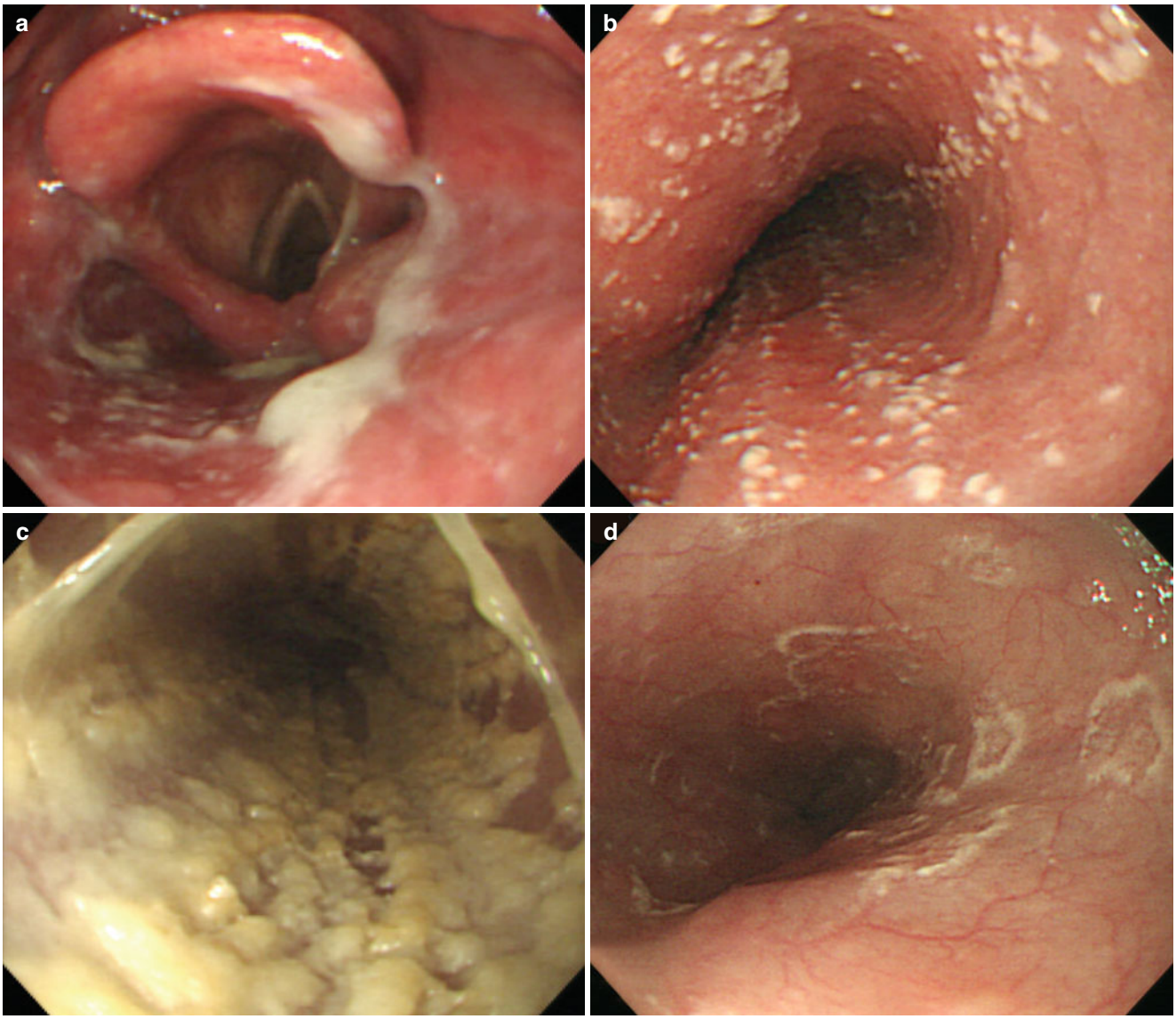

Fig. 3.5 Candida esophagitis. (**a**) Coexisting pharyngeal lesions help to diagnose Candida esophagitis. (**b**) Multiple white plaques. (**c**) Diffuse membranous white material. (**d**) Atypical lesions which resemble herpetic esophagitis

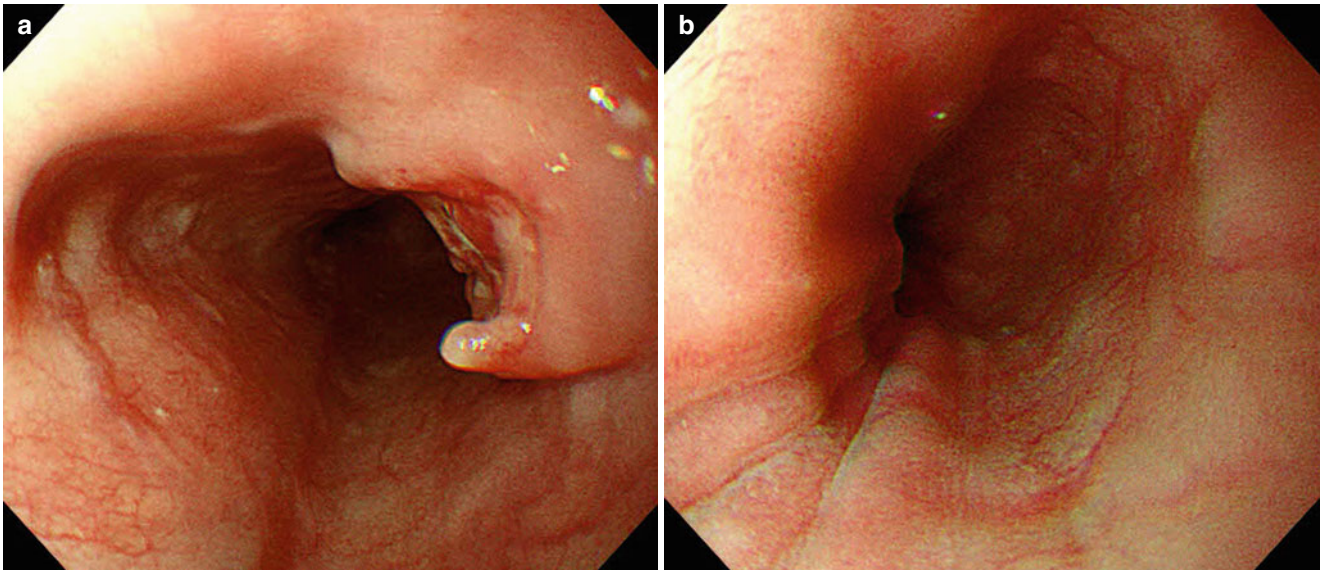

Fig. 3.6 Tuberculous esophagitis. (**a**) A mass-like lesion about 2 cm in size with central ulceration is found at mid-esophagus. (**b**) After antituberculous treatment for 3 months, scar change of the lesion is noted

3.2 Noninfectious Esophagitis

Other noninfectious stimulants such as mechanical and chemical trauma, radiation, and immunologic reaction can cause esophageal inflammation [2].

3.2.1 Pill-Induced Esophagitis

Some drugs can directly injure the esophagus. Representative drugs include doxycycline, aspirin, potassium chloride, quinidine, emepronium, ascorbic acid, and ferrous sulfate. Prolonged contact of the caustic contents of the drugs with the esophageal mucosa seems to be the main mechanism of injury. Therefore, the site of injury is usually located in areas where the esophageal lumen is narrowed by compression with aortic arch or enlarged left atrium [3]. The esophagogastric junction is another frequently involved site. Sudden onset of odynophagia and retrosternal pain is typical. This type of esophagitis should be suspected when typical symptoms appear abruptly after improper ingestion of oral medication. The typical endoscopic appearance is variable-sized, well-demarcated, solitary or multiple ulcers with relatively normal surrounding mucosa (Fig. 3.7). Symmetrical "kissing-type" ulcers are frequent. Sometimes, longitudinal serpiginous ulcers can be observed. If the remnant of the offending pill is identified at the site of injury, it helps to confirm this diagnosis.

3.2.2 Contact Esophagitis

The long-term placement of a nasogastric tube can cause various complications such as nasal ulcer, aspiration pneumonia, electrolyte imbalance, diarrhea, and hyperglycemia. It also may induce esophagitis or esophageal stricture by either direct compression pressure or acid regurgitation. Longitudinal erosions or ulcers with mucosal edema according to the direction of nasogastric tube are typical endoscopic findings (Fig. 3.8).

3.2.3 Corrosive Esophagitis

Ingestion of corrosive substances can cause severe injury to the esophagus and the stomach. The severity and extent of damage depend on properties and amounts of the ingested substance and duration of tissue exposure. Ingestion of alkali usually damages the esophagus more than the stomach, while acids cause more severe gastric injury, because ingested alkali is partially neutralized by gastric acid in the stomach. After ingestion of alkali, the injury extends rapidly through the mucosa and esophageal wall. As a result, penetrating injury ("liquefaction necrosis") can occur within 2 days to 2 weeks (Fig. 3.9). In contrast, acidic substances frequently cause coagulation necrosis which limits the depth of penetration (Fig. 3.10). Upper GI endoscopy should be performed during the first 24 h after ingestion in order to evaluate the extent of damage. Usual findings include erythema, edema, bleeding, erosions, and ulcers. Endoscopically, corrosive injury can be classified as three degrees (Fig. 3.11). First-degree injury shows only mucosal hyperemia and edema, without exudates or ulcerations. As the injury is confined to mucosal layer, perforation or stricture formation is absent in this degree. Second-degree injury shows shallow erosions or deep ulcers with covering exudates and severe erythema. Third-degree injury includes transmural damage and extensive mucosal necrosis. In this degree, the considering risk of perforation means that endoscopy should be terminated before passing the lesion.

3.2.4 Radiation Esophagitis

Radiation therapy is widely used to manage bronchogenic lung cancer, metastatic breast cancer, esophageal cancer, and lymphoma. Radiation doses as low as 30 Gy may affect esophageal mucosa, especially basal epithelial layer, and can cause esophagitis. The endoscopic appearance of radiation esophagitis is nonspecific and depends on the extent and exposure time of the radiation (Fig. 3.12). In the acute state, erythema, edema, erosion, ulcer, exudates, and necrosis are common findings, while stricture, fistula, scar change, and telangiectasia may develop in the chronic stage. Coexistent fungal or viral esophagitis is not rare [4].

3.2.5 Eosinophilic Esophagitis

Eosinophilic esophagitis is a recently recognized disease and can be defined as an allergic inflammatory condition of the esophagus [5]. Characteristic symptoms include dysphagia, food impaction, or heartburn that are unresponsive to antireflux treatments. To confirm the diagnosis, a minimum of 15 eosinophils per high power field in esophageal biopsy is required. Although various findings such as ridges, linear furrows, white exudates, or multiple rings can be found at endoscopy, cases with normally appearing mucosa are not rare (Fig. 3.13).

3.2.6 Behçet's Disease-Associated Esophagitis

Behçet's disease is a rare immune-mediated systemic vasculitis, which usually presents with mucous membrane

ulceration and ocular problems. Recurrent oral aphthous ulcers, genital ulcers, and uveitis are main symptoms. However, it can also involve various visceral organs such as the GI tract and pulmonary, musculoskeletal, cardiovascular, and neurologic systems. Although terminal ileum, cecum, and ascending colon are commonly involved sites among the GI organs, esophagus also can be involved. The type of ulcers in this esophagitis is similar to those of the lower GI tract and shows relatively well-demarcated, geographic ulcers. Identification of synchronous ulcers in other sites is helpful to diagnose this disease (Fig. 3.14).

3.2.7 Skin Disease-Associated Esophagitis

In several pemphigoid dermatologic disorders such as pemphigus vulgaris, cicatricial pemphigoid, bullous pemphigoid, and epidermolysis bullosa, esophageal involvement may be a manifestation of those diseases. Edematous desquamated epithelial layer is a typical finding (Fig. 3.15).

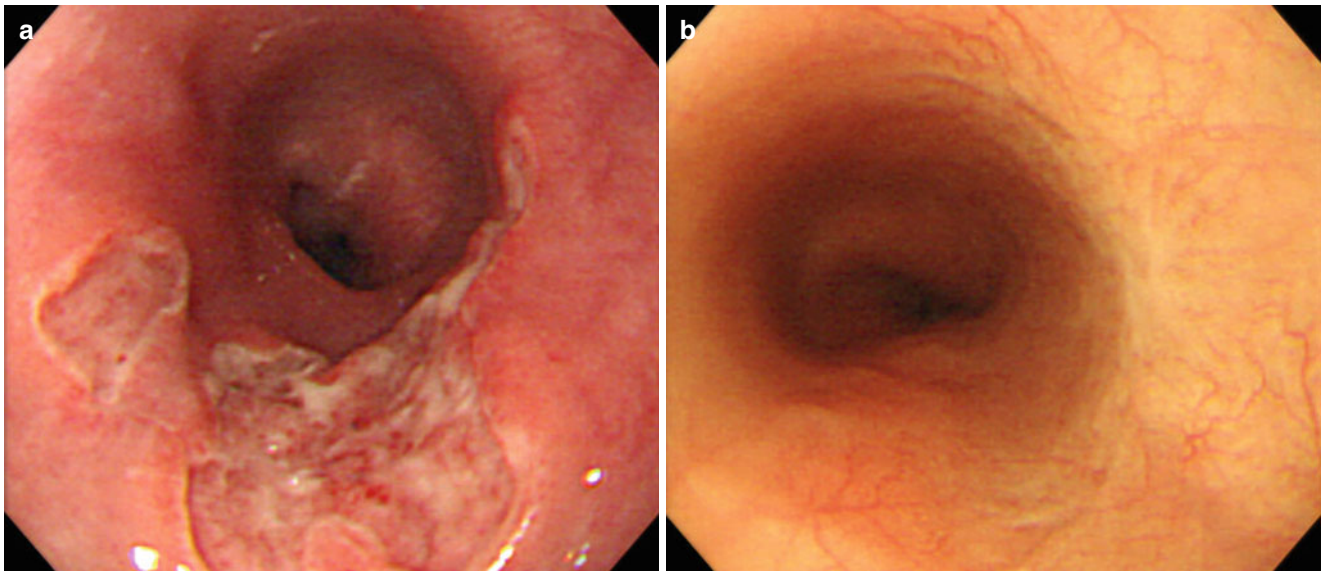

Fig. 3.7 Pill-induced esophagitis. (**a**) Three days after ingestion of an unknown medication, a small and a neighboring, large well-demarcated ulcer with intact surrounding mucosa are noted at mid-esophagus. (**b**) Scar change of the ulcer after 2 months

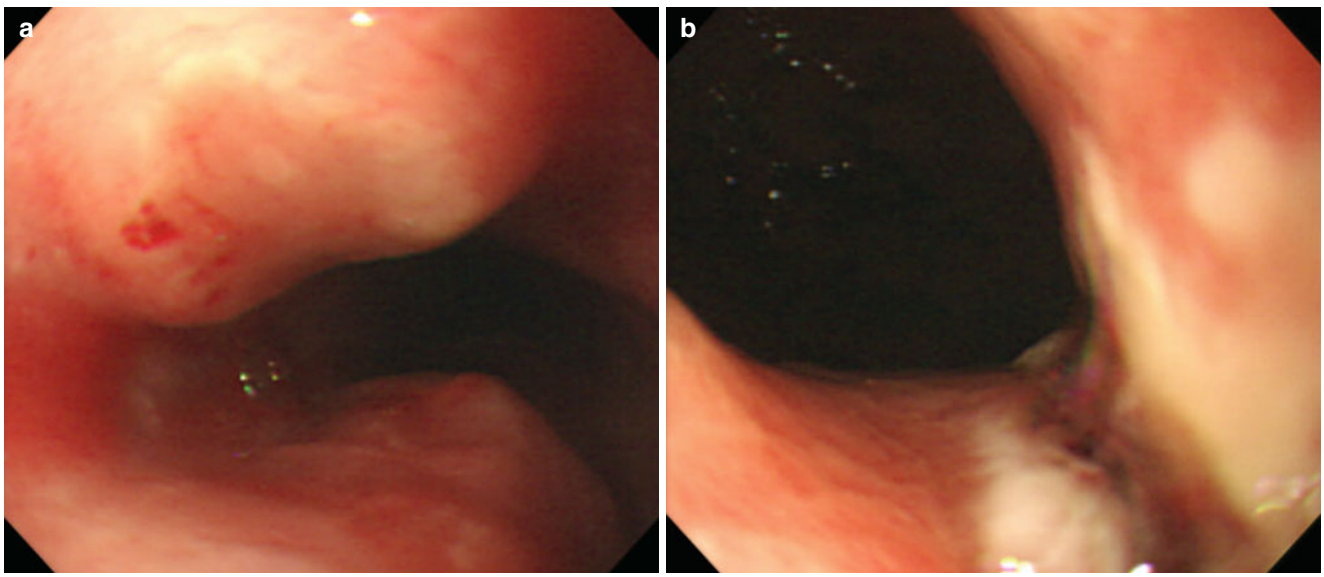

Fig. 3.8 Contact esophagitis. (**a**) Two longitudinally arranged kissing ulcers are found at protruded portions of mid-esophagus after long-term use of nasogastric tube. (**b**) Synchronous longitudinal ulcer is noted at the esophagogastric junction

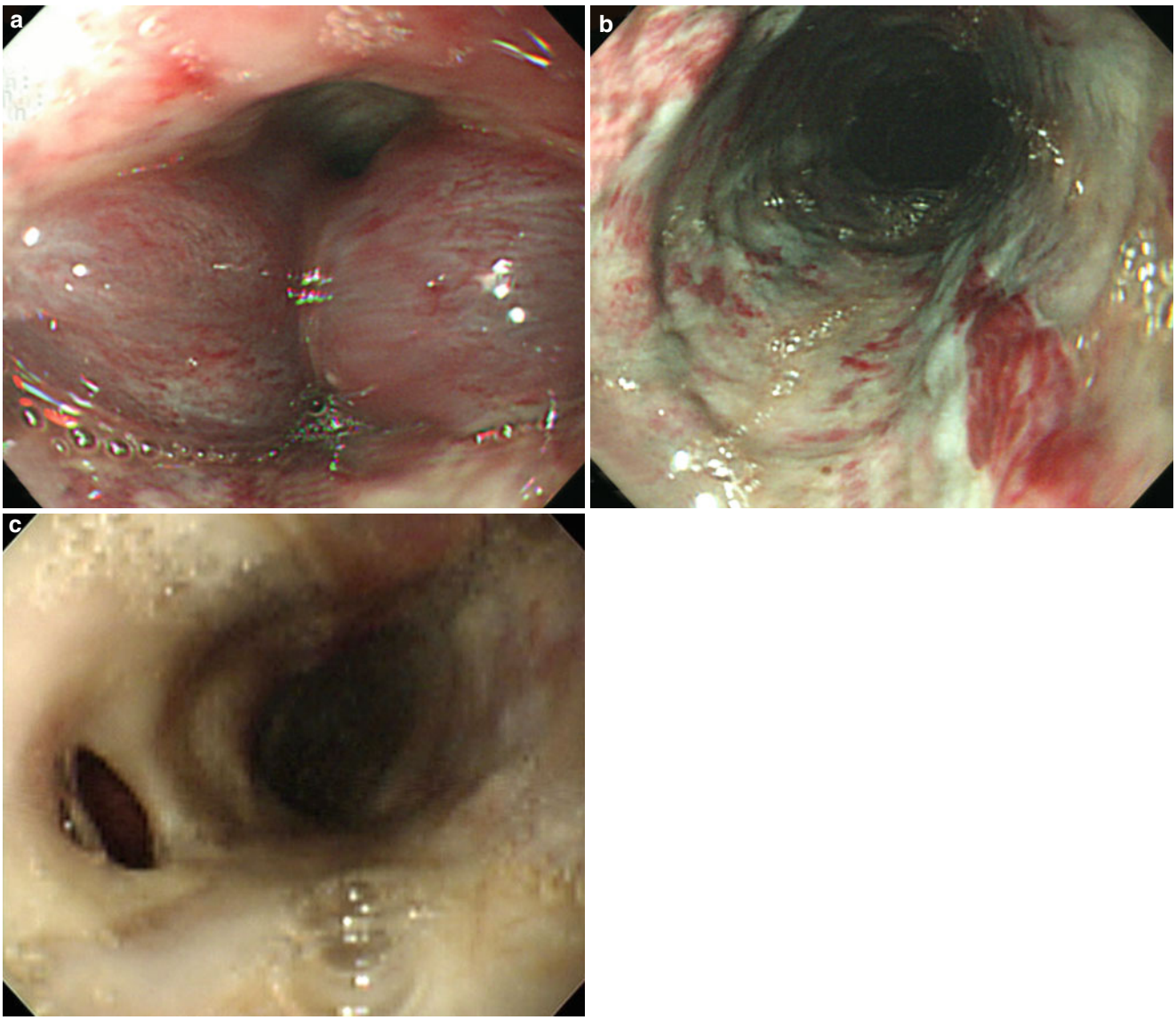

Fig. 3.9 Alkaline corrosive esophagitis. (**a**) Severe edema at pharynx, (**b**) extensive deep ulcer at almost the entire esophagus, (**c**) fistula formation after 20 days

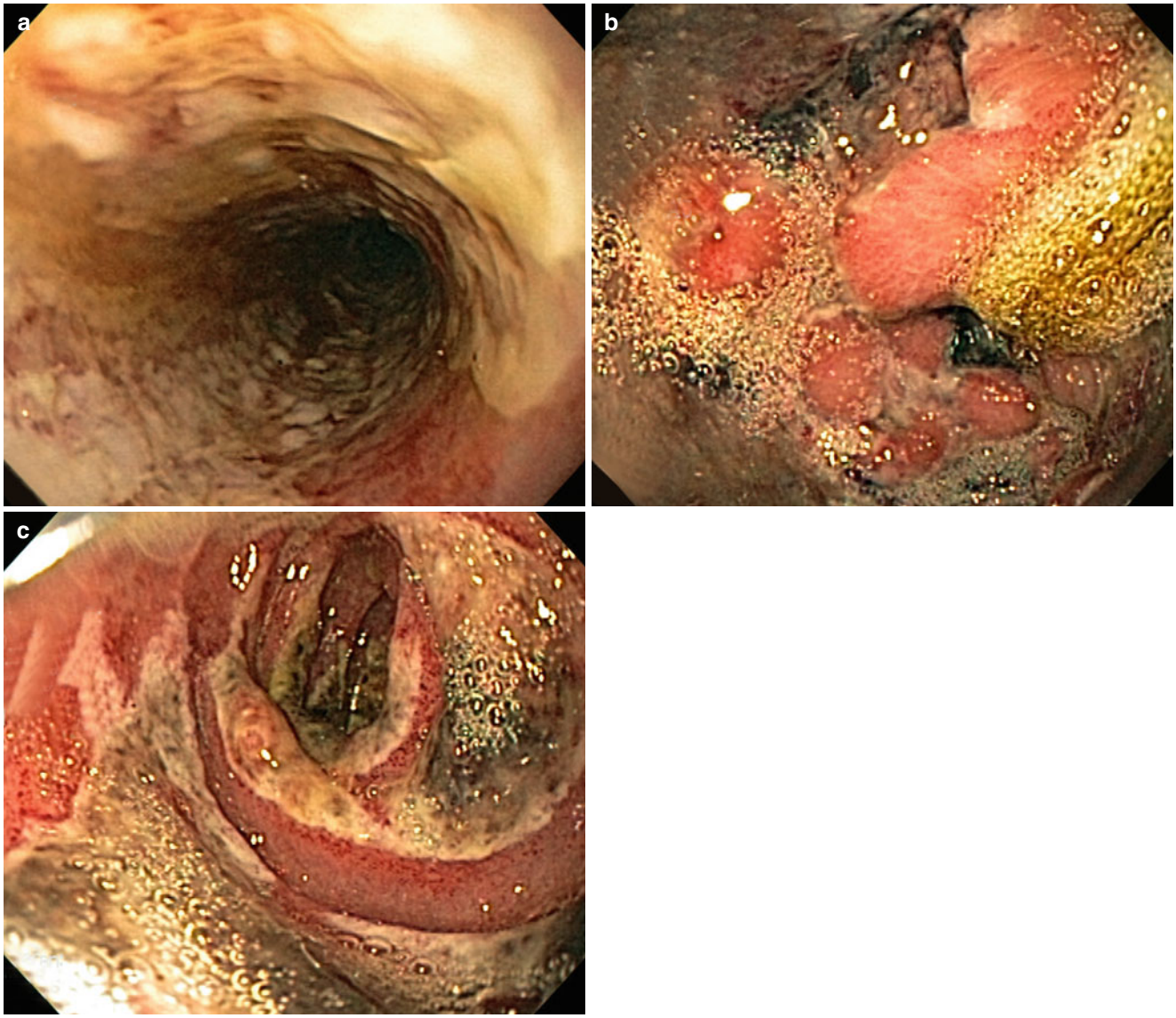

Fig. 3.10 Acidic corrosive esophagitis. (**a**) Relatively shallow injury with desquamation at esophagus. (**b**) Severe injury at stomach. (**c**) Extensive ulcer at duodenum

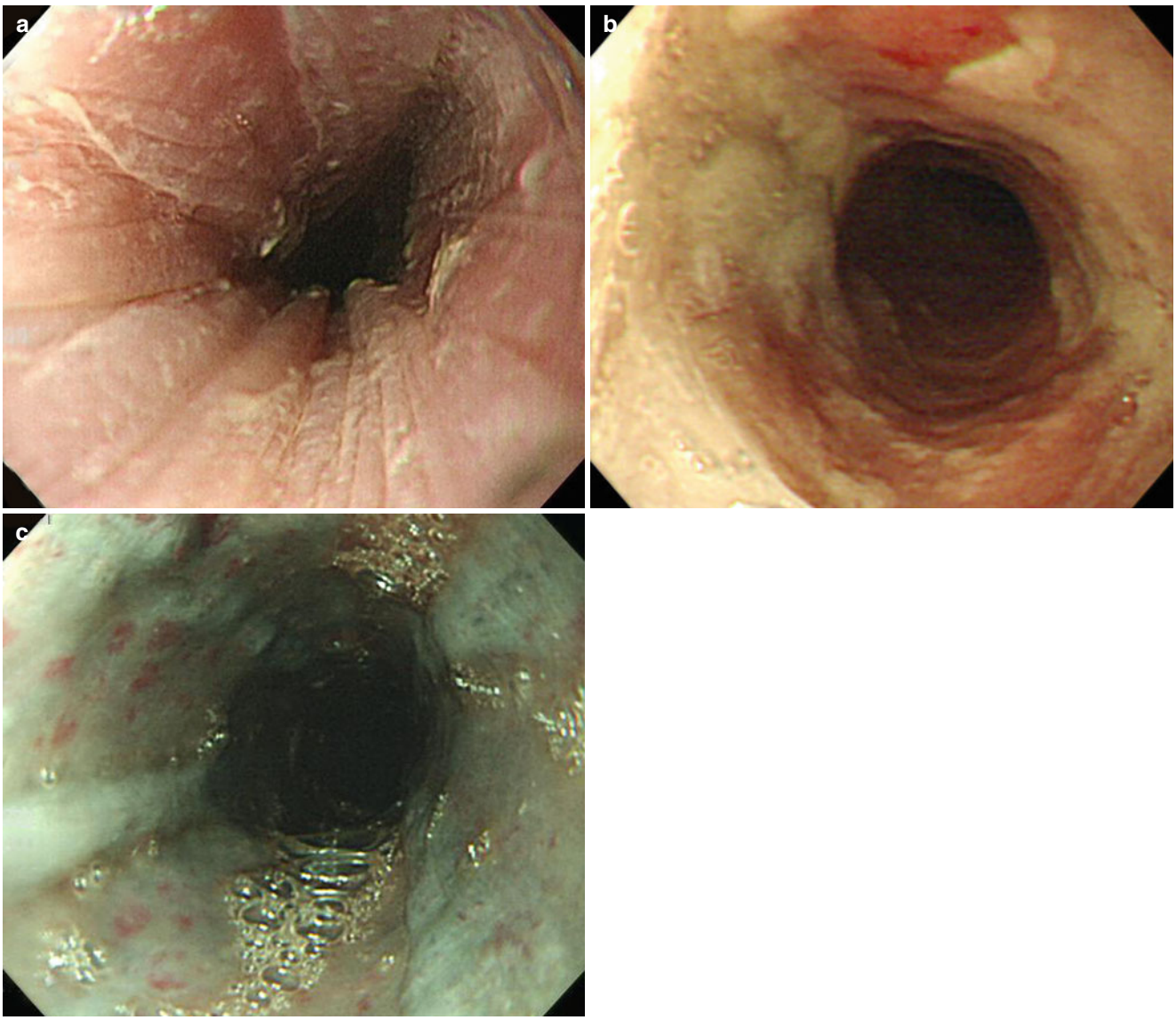

Fig. 3.11 Three degrees of corrosive injury. (**a**) Only mucosal hyperemia and edema in the first degree. (**b**) Shallow erosions or deep ulcers with covering exudates and severe erythema in the second degree. (**c**) Extensive mucosal necrosis in the third degree

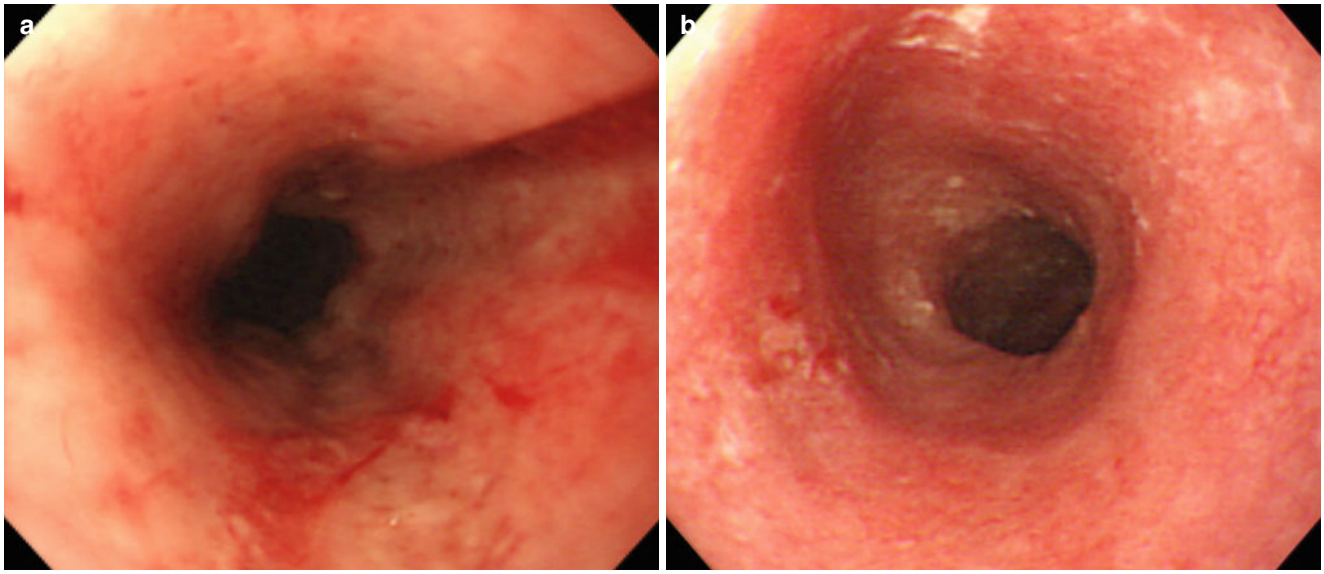

Fig. 3.12 Radiation esophagitis. (**a**) Shallow ulcers with surrounding edema and hemorrhage at upper esophagus. (**b**) Extensive edematous mucosa with attached exudates

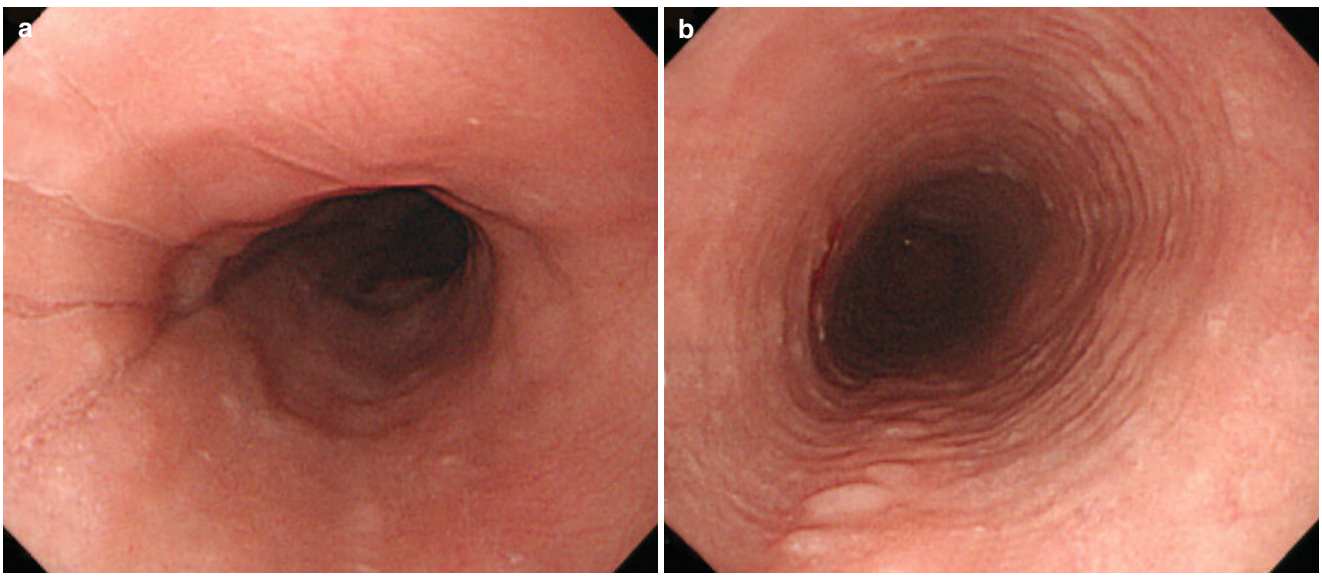

Fig. 3.13 Eosinophilic esophagitis. (**a**) Linear furrows, (**b**) multiple rings

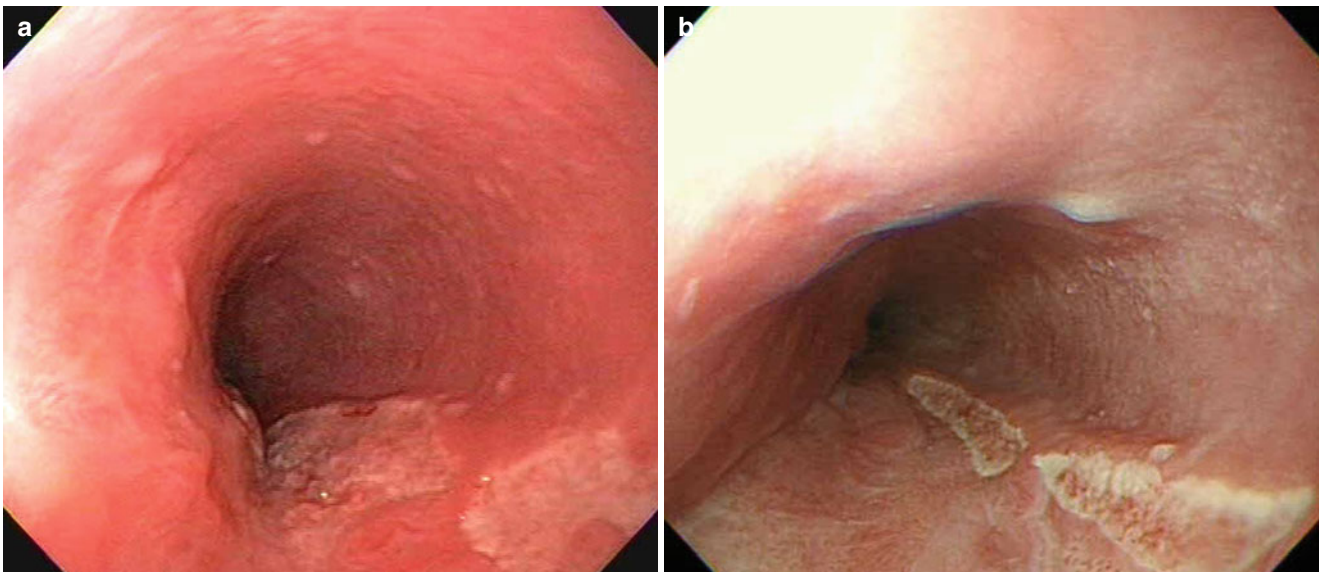

Fig. 3.14 Behçet's disease-associated esophagitis. (**a**) Geographically arranged deep ulcers with prominent demarcation. (**b**) Improving ulcers after steroid treatment for 2 months

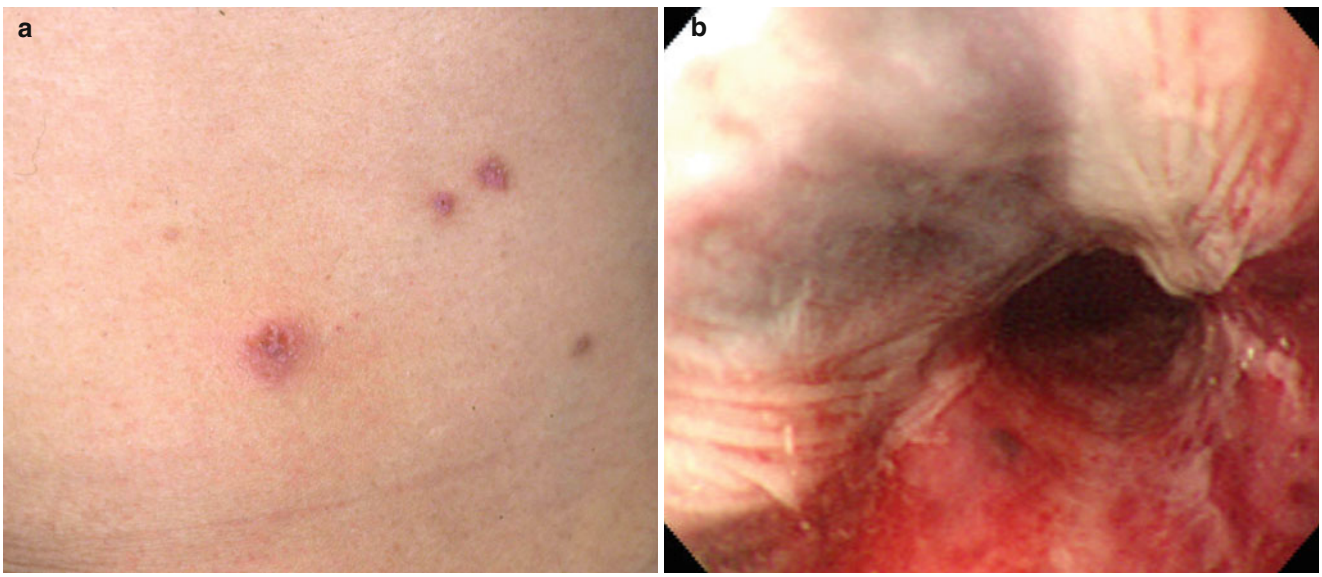

Fig. 3.15 Esophageal desquamation in a patient with bullous pemphigoid. (**a**) Skin, (**b**) esophagus

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