Diagnostic Techniques in the Esophagus

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7.1 Introduction

Even in the pediatric age group many diseases can affect the esophageal tract. The only procedure that permits direct visualization of the esophageal mucosa is upper endoscopy. Upper gastrointestinal (GI) endoscopy is employed widely not only for diagnostic but also for therapeutic purposes. This technique allows biopsy collection, which permits confirmation of conditions such as inflammation or infection [1]. Moreover, it permits therapeutic interventions such as dilations, sclerotherapy, endoscopic band ligation, and extraction of foreign bodies.

In these last 20 years, a new technique, endoscopic ultrasound (EUS) has been introduced to evaluate not only the wall of the upper or lower GI tract but also structures or organs in the immediate proximity of it. This is possible because EUS combines two modalities: endoscopic visualization and high-frequency ultrasound. The GI wall appears as a series of definable layers that corresponds to histological findings. EUS has a diagnostic and surgical role in the evaluation of GI diseases. In fact, it is possible to guide fine needles precisely through the gut wall into the surrounding structures [2].

7.2 Preparation and Technique of Endoscopy

With regard to fasting before upper GI endoscopy, the American Society of Anesthe-siologists advises not consuming: clear liquid for 2 h, breast milk and from formula for 4 h, as well as non-human milk and solids for 6 h before elective sedation. In emergencies, the risks of sedation without appropriate fasting must be evaluated after consideration of the necessity of the procedure and the expected benefit *versus* the risks [3].

The American Heart Association recommends antibiotic prophylaxis for bacterial endocarditis for patients with complex cyanotic congenital heart disease undergoing high-risk procedures (e.g., upper GI endoscopy with sclerotherapy and dilation of strictures) but it is not recommended for routine endoscopy with or without biopsy [4].

Before upper GI endoscopy, it is mandatory to obtain informed consent from parents or legal guardians if the patient is under 18 years old. Medical history, medication history, allergy assessment, age and weight must also be recorded. Physical examination (including a

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focused airway examination) should be done to reduce the complications of deep sedation in children because hyper-reactive airways are observed during and for several weeks after upper respiratory infections [5]. Moreover, if surgery is being considered, the hematocrit must be evaluated, coagulation assays carried out and blood grouping must be done in case transfusion is required in the case of hemorrhagic complications.

Preparation for upper GI endoscopy may differ from that seen in adults. A topical anesthetic spray in the pharynx of a young infant is avoided and bite blocks are usually not required in edentulous infants. Intubation of the esophagus has to be done under direct visualization [6, 7].

There is no standard practice for anesthesia in children undergoing GI endoscopy. Sedation for upper GI endoscopy can vary from conscious sedation with benzodiazepines (e.g., midazolam) to deep sedation with propofol to general anesthesia with orotracheal intubation. General anesthesia should be considered necessary for highly complicated procedures such as removal of foreign bodies and for patients at high risk for cardiovascular complications [8]. During endoscopy, baseline vital signs (heart rate, oxygenation) should be monitored and routine oxygen administration provided because of higher oxygen consumption in children, with consequent oxygen desaturation [9].

7.3 Indications for Upper GI Endoscopy

The indications for upper GI endoscopy in the pediatric population are based on guidelines set by the North American Society for Pediatric Gastroenterology and Nutrition in 1996. With respect to esophageal disorders, Squires et al. stated that diagnostic upper GI endoscopy is indicated: in active, persistent or recurrent bleeding in the GI tract (especially to differentiate between non-variceal and variceal bleeding); in dysphagia; in odynophagia; if there is a persistent refusal to eat; in persistent chest pain; if known or suspected ingestion of a caustic material has occurred; if there is persistent vomiting of unknown cause.

Conversely, upper GI endoscopy is not indicated for uncomplicated gastroesophageal reflux, uncomplicated functional abdominal pain, or radiographic findings of uncomplicated gastroesophageal reflux. Upper GI endoscopy is contraindicated for a perforated viscus. Sequential or periodic upper GI endoscopy may be indicated for surveillance for Barrett's esophagus (BE) as well as for the follow-up of: certain types of ulcers; mucosal abnormalities if they are likely to alter management; the adequacy of prior sclerotherapy or other variceal treatment.

Endoscopy can also have a surgical role. It can be indicated: for sclerotherapy or banding of esophageal varices; during or after a bleeding episode; for dilation; for treatment of persistent bleeding that is unresponsive to medical therapy; for removal of foreign bodies in the esophagus. or emergently for button batteries. Endoscopy is not indicated for sclerotherapy or banding of esophageal varices before the first documented variceal bleed [10].

7.4 Clinical Features of Esophageal Disease

7.4.1 Foreign Bodies in the Esophagus

Infants put almost everything into their mouths, and toddlers eat just about anything. Most foreign-body ingestions occur in children between the ages of 6 months and 3 years [11]. Fortunately, most foreign bodies pass spontaneously. Only 10–20% of subjects will require endoscopic removal, and <1% require surgical intervention [12]. Although mortality from foreign-body ingestion is extremely low, deaths have been reported [12, 13].

Most children with esophageal foreign bodies tell their parents of the ingestion, or the ingestion is witnessed by the parents or report-

ed to them. In these settings, they are often asymptomatic [14, 15]. If symptoms occur, they are often related to the location of the foreign body. Older children may localize the sensation of something "stuck" to the neck or lower chest, suggesting irritation in the upper or lower esophagus, respectively. Patients of any age may present with refusal of feeding or dysphagia, drooling, or respiratory symptoms (including wheezing, stridor, or choking). Esophageal foreign bodies tend to lodge in areas of physiological narrowing, such as the upper esophageal sphincter (cricopharyngeus muscle), the level of the aortic arch, and the lower esophageal sphincter [14]. Objects that appear in the middle portion of the esophagus are more likely to represent esophageal disease, such as a stricture. Similarly, children presenting with impaction of a food bolus commonly have underlying esophageal disease (e.g., a stricture) that is directly responsible for the impaction [16]. Previous surgery or congenital malformations (e.g., tracheoesophageal fistula) pose an increased risk as sites for obstruction. Longstanding esophageal foreign bodies may cause weight loss or recurrent aspiration pneumonia. They also can damage the mucosa and lead to strictures, or erode the esophageal wall, creating a fistula with the trachea or other nearby structures. Sharp objects may perforate the esophagus, resulting in neck swelling, crepitus, or pneumomediastinum.

Careful history-taking and physical examination are the keystones for diagnosing an esophageal foreign body and for the prevention of its complications [17]. Imaging is used to confirm the findings and to localize the site of the foreign body. Urgent intervention is indicated if any of the following warning signs are present:

- the ingested object is sharp, long (>5 cm), consists of multiple magnets, and is in the esophagus or stomach;
- a disk battery is in the esophagus (and in some cases in the stomach);
- there are signs of airway compromise;
- there is evidence of near-complete esophageal obstruction (e.g., patient cannot swallow secretions) [18].

For blunt foreign bodies without the characteristics shown above that are lodged in the esophagus in an asymptomatic patient, observation for 12–24 h is reasonable because spontaneous passage often occurs [19, 20].

Objects lodged for >24 h or for an unknown duration should be removed promptly. After this period, complications are more likely to occur. Flexible endoscopy is preferred in most circumstances because the foreign body can be directly visualized and manipulated, and the surrounding GI tract can be examined for potential complications [21–23].

This procedure is undertaken under conscious sedation or general anesthesia depending upon the patient's age, ability to cooperate, as well as the type and number of objects to be removed. The endoscopist should have a complete array of equipment to grasp the foreign object: rat-tooth forceps, alligator forceps, polyp snare, retrieval net, and helical baskets. It is helpful to practice grasping a duplicate of the foreign body using the retrieval tools before beginning the procedure. A foreign body protector hood is the preferred method of protecting the esophagus if the object is sharp or pointed [24].

Coins are by far the most common foreign body ingested by children [25]. A small percentage of ingested coins become lodged in the esophagus, and these can cause serious complications (including aspiration) if they are not removed [26]. If a coin is visualized in the esophagus and the patient is asymptomatic, the child can be observed for ≤24 h after ingestion of the coin. In such patients, 20–30% of coins will pass into the stomach spontaneously during the observation period (two-thirds of these during the first 8 h). The esophageal coin should be removed promptly if the patient is symptomatic or if the time of ingestion is not known (Fig. 7.1). If the child is asymptomatic and the coin does not pass spontaneously by 24 h after ingestion, it should be removed.

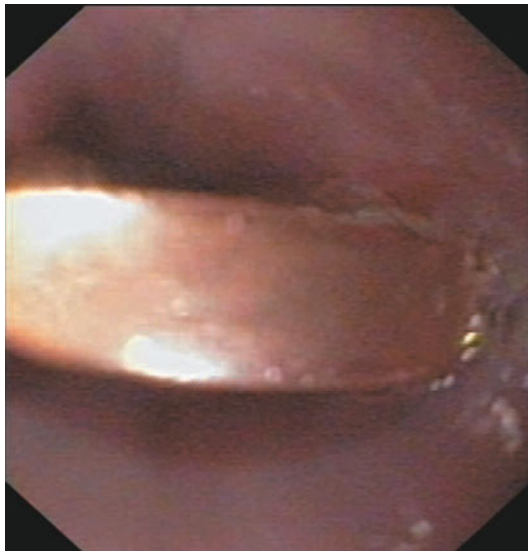

Fig. 7.1 Coin in the proximal esophagus

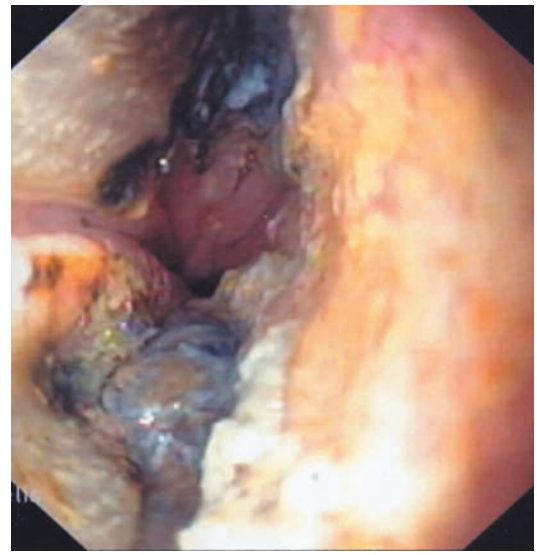

Fig. 7.2 Esophageal necrosis after button battery ingestion

Disk or "button" batteries: The number of ingestions of disk or button batteries is increasing substantially [27] and this is a medical emergency. In addition to direct-pressure necrosis, contact of the flat esophageal wall with both poles of the battery results in the conduction of electricity, resulting in liquefaction necrosis and perforation of the esophagus (Fig. 7.2). Retained batteries also can cause problems through leakage of caustic material (batteries contain a heavy metal such as mercury, silver and lithium, as well as a strong hydroxide of sodium or potassium) [28].

Sharp-pointed objects: The most common sharp-pointed objects ingested by children are straight pins, needles (Fig. 7.3) and straightened paper clips. Sharp-pointed objects lodged in the esophagus represent a medical emergency because of a high risk of perforation (15–35%). If the object is in the esophagus, it should be removed immediately. Endoscopic retrieval of sharp objects is accomplished with use of retrieval forceps or polypectomy snares [29]. The risk of mucosal injury during retrieval of a sharp object can be minimized by orienting the object with the sharp-end trailing during extraction and using a foreign body protector hood on the end of the endoscope or (in older children) an overtube [17].

Impacted meat or other types of food bolus are relatively rare in children. They usually present as dysphagia that begins acutely while eating. In children presenting with food impaction, there is a higher incidence of underlying esophageal pathology (strictures, achalasia, esophageal motility disorders) as compared with children with other esophageal foreign bodies [30]. Reflux esophagitis and eosinophilic esophagitis (EE) also predispose to food impaction [30, 31]. The optimal approach to removal of a food bolus depends on the location and consistency. Some authors find that polypectomy snares or retrieval nets fitted to the end of the endoscope are valuable for removal of a food bolus. The food bolus can be removed *en bloc* or in a piecemeal fashion. Once reduced in size, the bolus may be gently pushed into the stomach using the tip of the endoscope. Because food impaction is often caused by an underlying mucosal abnormality such as esophagitis or strictures, esophageal mucosal biopsies are recommended at the time of endoscopic dis-impaction [32].

Ingestion of magnets has become a serious health hazard in children [33–35]. Two or

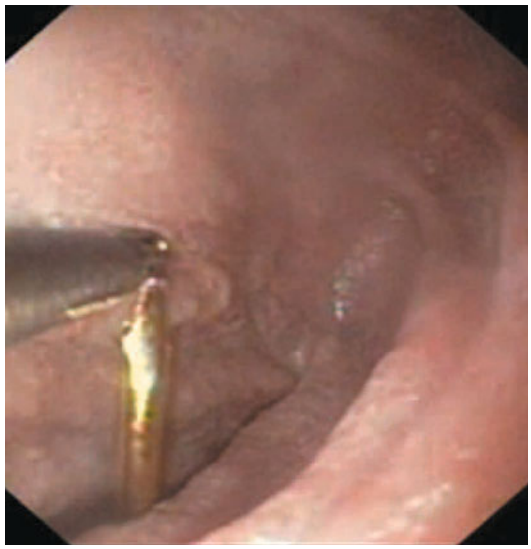

Fig. 7.3 Nail in duodenum

more strong magnets may attract across layers of bowel, leading to pressure necrosis, fistulas, volvulus, perforation, infection, or obstruction; this may result in serious consequences (including intestinal resection). Suspected magnet ingestion requires urgent evaluation. Radiographs of the neck and abdomen should be conducted (including a lateral view). Management depends on the timing, location, type and number of magnets, but magnets in the esophagus or stomach should be promptly removed *via* endoscopy.

Objects with high lead content: Acute lead toxicity may occur in children ingesting objects with high lead content, including lead weights used for fishing ("sinkers"), curtain weights, air-rifle pellets, and some toys or medallions. Objects suspected to have high lead content should be removed from the esophagus or stomach as quickly as possible. Use of proton pump inhibitors (PPIs) may decrease the dissolution of lead [36].

7.4.2 Caustic Ingestion

In infants and children, caustic ingestion is usually accidental, whereas in adolescents and adults it is usually deliberate. In ≈90% of cases the ingestion occurs at home and the exposure is to a single substance [37]. The literature suggests that household bleach accounts for 30–40% of caustic ingestions, laundry detergents for 20%, and acids and alkalis from cleaning products (e.g., oven, toilet, tile, drain) account for ≥50% [38, 39]. Caustic ingestion can cause severe damage to the esophageal mucosa, and the extent and the severity of the damage can depend upon the: type of caustic agent; amount and concentration of ingested caustic material; duration of contact between the mucosa and caustic agent [40, 41].

Alkalis cause liquefaction necrosis with deep penetration into the wall, and this can lead to perforations. Acid ingestion can cause coagulation necrosis, which limits the extent of penetration because the coagulum on the mucosal surface can limit the penetration of the caustic substance into the wall [42]. There is no correlation between the presence or absence of symptoms and the severity of injury to the GI tract, but an increased number of symptoms correlate with a greater likelihood of significant injury [43].

Also, the presence or absence of oral lesions does not correlate with esophageal injury. The most common symptoms are dysphagia, drooling, feeding refusal, retrosternal pain, abdominal pain and vomiting [37]. Symptoms involving the airway are less common (although dyspnea is associated with a high risk of significant GI injury) [43].

If patients have a strong history of ingestion, have oral burns, or are symptomatic, the most reliable method to establish the presence and extent of lesions is upper GI endoscopy (which must be carried out within 24 h). In asymptomatic patients, some authors suggest that upper GI endoscopy should be done anyway, but other authors suggest observation and liquid intake [37]. Upper GI endoscopy is useful to grade esophageal injury (Fig 7.4) and therefore to decide the most appropriate therapy. There are four grades of esophageal injury according to endoscopy: 1 (edema and

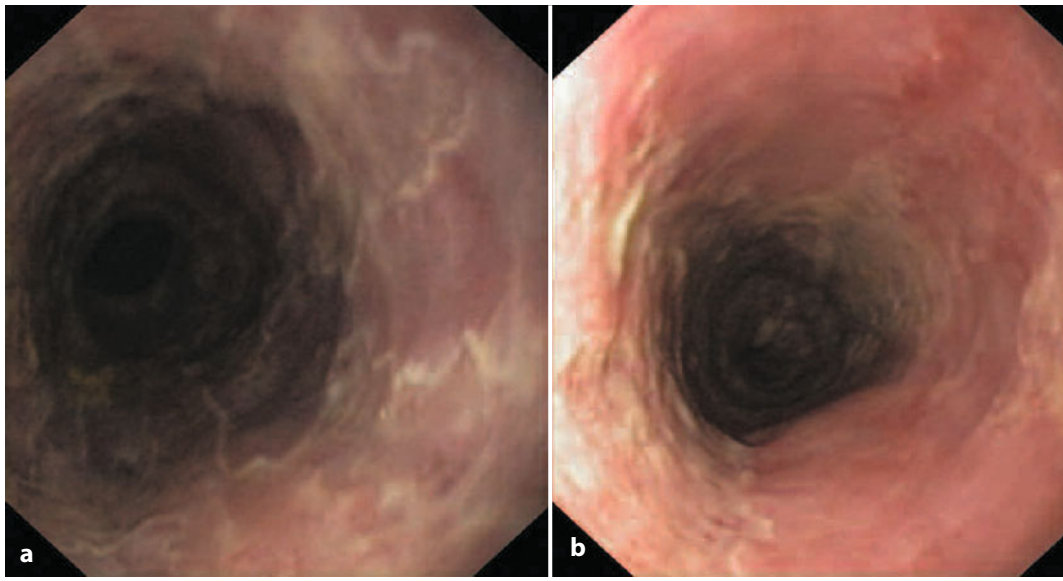

Fig. 7.4 a,b Esophagitis after caustic ingestion

erythema); 2 (linear ulceration and necrotic tissue with whitish plaques); 3 (circumferential injury which may be transmural with mucosal sloughing); and 4 (perforation).

Grade-1 lesions are present in 60–80% of patients who have an esophageal injury [44]. Grade-2 and -3 injuries can determine long-term consequences such as strictures which may occur in ≤2–38% of patients with caustic ingestion and in ≤3–57% of patients with documented esophageal burns. About 80% of patients with strictures will present with obstructive symptoms within 2 months from the ingestion [45].

The endoscopic treatment of patients with strictures comprises esophageal dilation or esophageal stenting. Patients with grade-4 lesions have a poor prognosis due to systemic complications [43]. Other complications secondary to caustic ingestion are dysphagia, esophageal motility abnormalities, esophageal perforations (which can also be due to esophageal dilations). Esophageal perforations can cause pneumothorax, pneumomediastinum, the need for esophageal or gastric surgery, or cause death [46]. Also esophageal carcinoma (adenocarcinoma, squamous cell carcinoma) is a late (but serious) complication of severe caustic injury, with a prevalence of 2–30%, and the time interval between ingestion and tumor detection is 16–42 years [37].

In patients with caustic ingestion, ipecac or oral dilutions (e.g., milk, water, neutralizing agents) are contraindicated because vomiting may lead to additional esophageal injury if gastric contents come into contact with the esophageal mucosa. Nasogastric tubes should be placed under direct vision in patients with extensive circumferential burns. They can provide a route for nutritional support during the healing phase, and they can be placed as stents to keep the esophagus open if stricture development is anticipated. Treatment with corticosteroids is controversial and is usually confined to patients with airway symptoms. This treatment does not seem to protect the airway against the development of esophageal strictures. If corticosteroids are needed, concomitant administration of broad-spectrum antibiotics is required [47].

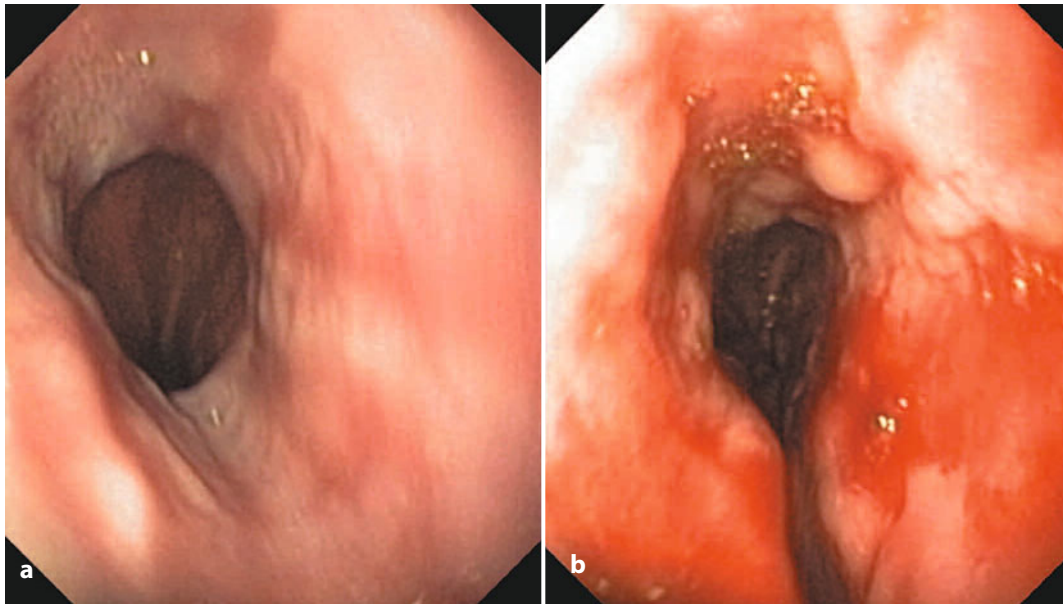

Fig. 7.5 a,b Esophagitis in GERD

7.4.3 Gastroesophageal Reflux (GER)

The passage of gastric contents into the esophagus (GER) is a normal physiological process that occurs in healthy infants, children, and adults. Most episodes are brief and do not cause symptoms, esophageal injury, or other complications. In contrast, gastroesophageal reflux disease (GERD) occurs if the reflux episodes are associated with symptoms or complications. The range of symptoms and complications of GERD in children vary with age.

GER is extremely common in healthy infants, in whom gastric fluids reflux into the esophagus ≥30 times daily [48]. Frequent episodes of regurgitation during infancy may be associated with an increased likelihood of having GERD symptoms in later childhood [49]. Infants can develop symptoms such as failure to thrive, hematemesis, and anemia, suggesting the possibility of GERD. A manifestation of GERD consisting of arching of the back, torsion of the neck, and lifting up of the chin (Sandifer syndrome) can be confused with torticollis.

Preschool age children with GERD may present with intermittent regurgitation. Less commonly, they may have respiratory complications such as persistent wheezing. Decreased food intake without other complaints may be a symptom of esophagitis in young children. All of these symptoms are non-specific and not sufficient to make a definitive diagnosis of GERD.

The pattern of symptoms and complications in older children and adolescents resembles that seen in adults. The cardinal symptoms are chronic heartburn and/or regurgitation [50]. Complications of GERD, including esophagitis (Fig 7.5), strictures, Barrett's esophagus, and hoarseness due to reflux laryngitis, may also be seen. Specific testing should be guided by the type of symptoms and their severity.

Monitoring of esophageal pH permits assessment of the frequency and duration of esophageal acid exposure and its relationship to symptoms even if is rarely useful in establishing the diagnosis of GER in infants because it does not detect anatomical abnor-

malities or directly measure the severity of esophagitis [51, 52]. Esophageal pH monitoring or multichannel intraluminal impedance monitoring (MII) can be useful in atypical symptoms of reflux, in reflux symptoms not responsive to medical or surgical therapy, or in infants with apnea or apparent life-threatening events [53].

The test is undertaken by the transnasal passage of a microelectrode containing a pH sensor into the lower esophagus. The pH electrode is positioned according to a formula that takes into account the length of the child. A device worn by the patient records the exposure to esophageal acids during monitoring. The procedure is considered to be very safe, but keeping the probe in place may be difficult in toddlers and uncooperative children. The results of a pH probe study are influenced by the type of recording device, its exact position within the esophagus, diet, position of the patient, and activity during the study. Interpretation of results after longer periods of monitoring (24 h) is more reliable than after shorter periods (e.g., 12 h), although longer periods of monitoring may not always be feasible [54]. In many centers, esophageal pH monitoring is combined with MII to allow measurement of weakly acidic and alkaline reflux episodes. In a trial comparing the two techniques, combined MII–pH monitoring detected associated symptoms twice as often as pH monitoring alone [55].

Endoscopic evaluation of the upper GI tract is indicated for patients: in whom esophagitis or gastritis is suspected; with recurrent regurgitation after 2 years of age; with dysphagia, odynophagia, or a history of food impaction. Endoscopy permits visualization of the esophageal epithelium as well as histological evaluation to determine the presence and severity of esophagitis and complications such as strictures or BE, and to exclude other disorders such as EE, allergic esophagitis, or infectious esophagitis. An esophagus that appears normal at endoscopy does not exclude the presence of GERD. Sensitivity can be increased with mucosal biopsies, which may reveal intraepithelial eosinophils or other histological findings consistent with GERD [56]. Biopsies of the esophagus, stomach or duodenum may reveal inflammation characteristic of dietary protein intolerance or other systemic disorders. Cellular injury stimulates cell proliferation, the morphological equivalent of which is thickening of the basal cell layer and elongation of the papillae of the epithelium. Findings of basal zone hyperplasia are uncommon in young children, and other histological features, such as the presence of neutrophils and eosinophils, and dilated vascular channels in the papillae of the lamina propria, are more typically seen in the pediatric population [57]. Endoscopy can be carried out in infants, toddlers, and older children. Procedure-related complications of diagnostic endoscopy and biopsy appear to be rare [58]. Complications may occur due to over- or under-sedation [59]. The most common complications are sore throat or hoarseness, which occur in 35% of patients.

For uncomplicated reflux, intervention is not required for most infants. Over-feeding and exposure to tobacco smoke should be avoided. A trial of a milk-free diet and thickening of feeds may be considered if the reflux causes significant adverse effects on quality of life [60]. Infants younger than 12 months of age should be placed in the supine position for sleep, even if they have reflux. The prone position tends to reduce reflux [61] but is also associated with a higher risk of sudden infant death syndrome (SIDS). This risk outweighs the potential beneficial effect of sleeping in the prone position on reflux [62].

The type of lifestyle changes that may be beneficial depend upon the patient's age and symptom characteristics. Weight loss or elevation of the head of the bed improves laboratory measures of reflux but there is no clinical evidence that they consistently improve reflux symptoms [63].

Acid-suppression and prokinetic medications have a limited role in the treatment of infants with regurgitation. They are not valuable in the treating children <1 year of age with un-

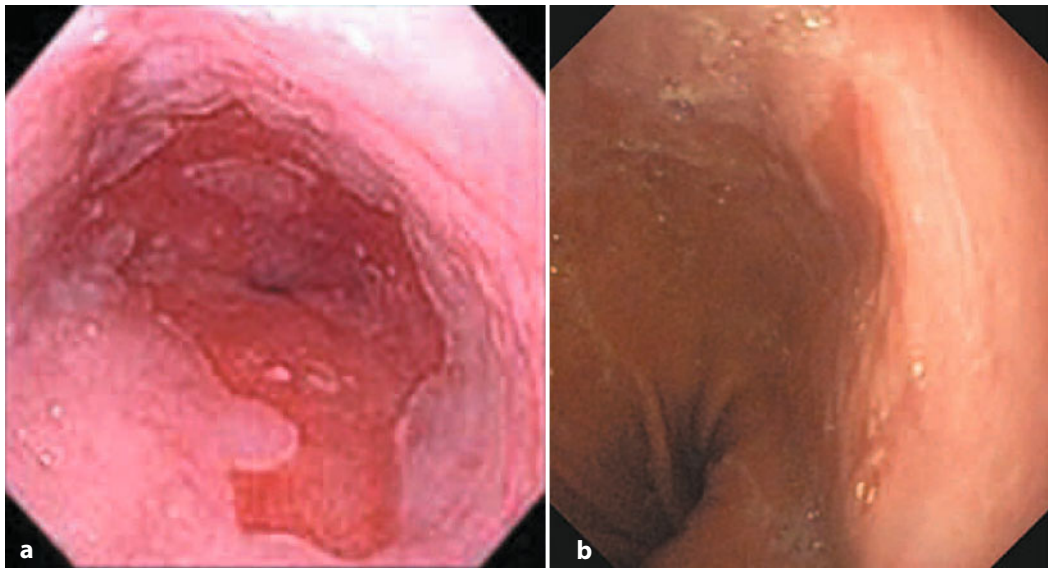

Fig. 7.6 a,b Barrett's esophagus

complicated GER ("happy spitters"). Many infants with symptoms suggestive of GERD will improve over time with conservative measures alone [64]. Infants with esophageal atresia, chronic neuromuscular diseases, chronic respiratory disease or diaphragmatic hiatal defects are more likely to develop erosive esophageal disease over time, and may benefit from early PPI treatment if indicated [65].

If acid suppression is chosen as a treatment or for a limited trial, a PPI that blocks acid secretion by irreversibly binding to and inhibiting the hydrogen–potassium ATPase pump is generally preferred [66]. Infants and younger children metabolize PPIs more rapidly than older children and require higher per-kilogram dosing than older individuals [67].

Histamine type-2 receptor antagonists (H2RAs) have moderate effects on GER as measured by symptom relief and mucosal healing. However, they are less effective than PPIs. Prokinetic agents enhance esophageal peristalsis and accelerate gastric emptying, providing a *rationale* for their use in GERD. They should be considered only in carefully selected patients, including those who have failed anti-secretory therapy (PPIs or H2RAs). They have a minimal role in the treatment of GER in this age group [60].

GER must be diagnosed correctly because it probably plays a major part in the development of BE through repeated mucosal damage. Reflux symptoms for >5 years increase the risk of Barrett esophagus (BE) by threefold, and by sixfold if symptoms occur for >10 years in adults [68]. BE is associated with a 30-fold increase in the risk on esophageal adenocarcinoma in adults, so an adequate and early diagnosis as well as surveillance even in children is important [69].

BE can be diagnosed only by using upper GI endoscopy to obtain biopsies of the esophagus. The diagnosis is based on the endoscopic findings of columnar epithelium lining the distal esophagus (Fig. 7.6) and confirmed by intestinal metaplasia in esophageal biopsy specimens [70]. Multiple closely spaced biopsies are required to minimize sampling error, and to detect possible dysplasia. The literature suggests that four-quadrant biopsies every 1 cm for circumferential metaplastic segments is best [71].

There are no firm guidelines for surveillance in children. However, in adults it is rec-

ommended to repeat endoscopy with biopsy within 1 year. However, if dysplasia has been diagnosed it is suggested to repeat endoscopy with biopsy after 6–12 months in the case of low-grade dysplasia, followed by yearly endoscopy if there is no progression [72].

7.4.4 EE

The esophagus, which is normally devoid of eosinophils, is an immunologically active organ that can recruit eosinophils in response to various stimuli [73]. EE is defined as "a chronic, immune/antigen-mediated, esophageal disease characterized by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation" [74]. The incidence of EE appears to be increasing. This may be partly due to an increased recognition of the disorder [75]. Among children, the disease is more common in boys (71% in the series described above) [76].

The pathogenesis of EE is incompletely understood but includes environmental and genetic factors. Eosinophils establish themselves as permanent residents of the GI tract early during embryonic development (even though they are not normally found in the esophagus). Eosinophil recruitment is observed in various inflammatory or infectious conditions, such as inflammatory bowel disease, GER, and after exposure to food allergens [77–79]. The manifestations of EE vary with age [80–82]. The most common presenting symptoms and the median ages at which they occur are:

- feeding dysfunction (2.0 years);
- vomiting (8.1 years);
- abdominal pain (12.0 years);
- dysphagia (13.4 years);
- food impaction (16.8 years).

There is a strong association between EE and allergic conditions such as food allergies, environmental allergies, asthma, and atopic dermatitis. It has been estimated that 42–93% of children with EE have another allergic disease [83–87]. An association with celiac disease (and response to a gluten-free diet) has been described [88]. In addition, an association with Schatzki ring has also been described [89] but the strength of this association is not clear.

The diagnosis of EE should be based upon symptoms, endoscopic appearance, and histological findings. In patients suspected of having EE, the first diagnostic test is typically an upper GI endoscopy with esophageal biopsies after 1–2 months of treatment with a PPI, though radiographic and laboratory findings may support the diagnosis. Other disorders that can cause esophageal eosinophilia, such as GERD, should be ruled out. Various morphological features in the esophagus have been described in patients with EE [90, 91]. Endoscopic findings (Fig. 7.7) include:

- stacked circular rings ("feline" esophagus);
- strictures (particularly proximal strictures);
- attenuation of the subepithelial vascular pattern;
- linear furrowing that may extend the entire length of the esophagus;
- whitish papules (representing eosinophil microabscesses);
- small-caliber esophagus.

Complications associated with endoscopy in patients with EE include esophageal perforation and mucosal tears [92, 93]. Esophageal biopsies from patients with EE show an increased number of eosinophils. Most patients have ≥15 eosinophils per high power field (HPF; peak value) in at least one biopsy specimen after taking a PPI. Esophageal eosinophilia in the absence of clinical features is not sufficient to make a diagnosis of EE. During endoscopy, biopsies should be obtained from the distal esophagus as well as the mid or proximal esophagus [94]. Two-to-four biopsies must be obtained from the distal esophagus, as well as another 2–4 from the mid or proximal esophagus.

Barium studies are not sensitive for diagnosing EE, but can help characterize anatomical abnormalities and provide information on the length and diameter of strictures [95, 96].

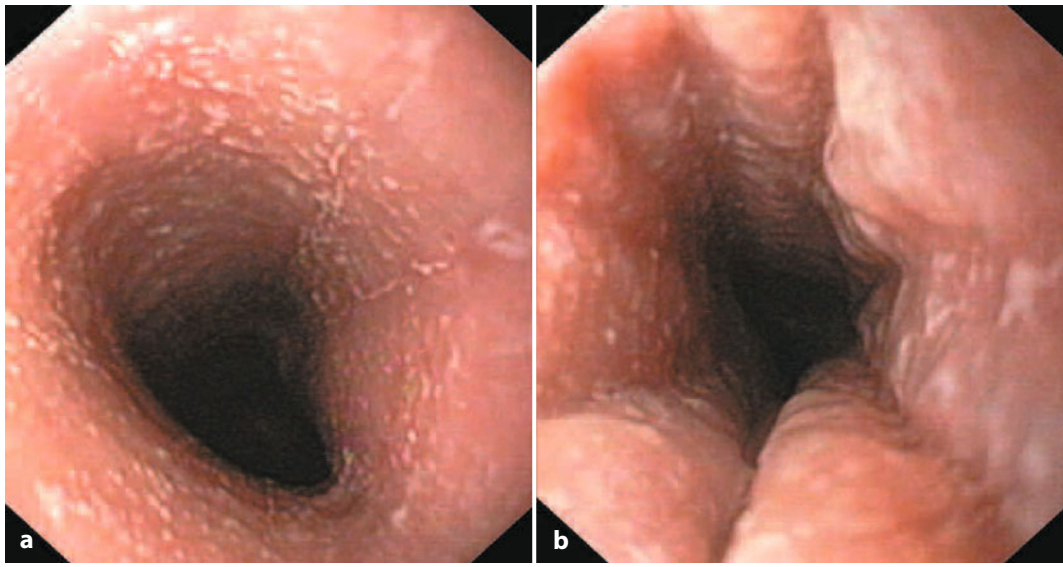

Fig. 7.7 a,b Manifestations of eosinophilic esophagitis

There are no diagnostic serum markers for EE. However, 50–60% of patients with EE will have elevated levels of IgE in serum (>114,000 units/L). Peripheral eosinophilia is seen in 40–50% of patients but is generally mild [97]. It decreases with topical glucocorticoid therapy [76].

The differential diagnoses include conditions that can cause morphological or histological findings that resemble EE. These include GERD, recurrent vomiting due to other causes, parasitic and fungal infections, congenital rings, Crohn's disease, periarteritis, allergic vasculitis, drug injury, connective tissue diseases, bullous pemphigoid, pemphigoid vegetans, graft-versus-host disease, achalasia, drug hypersensitivity, celiac disease, vasculitis, carcinoma, and several causes of peripheral eosinophilia in which the esophagus (along with other organ systems) may become involved. The most common consideration in the differential diagnosis of EE is GERD. As noted above, large numbers of eosinophils (>100/HPF) may be seen in association with GERD. Because of the association of GERD with esophageal eosinophilia, biopsies for EE should be obtained after 1–2 months of treatment with a PPI or after an esophageal pH study has excluded reflux [98].

The management of EE includes dietary, pharmacological, and endoscopic interventions [99]. Commonly used treatments include:

- elimination and elemental diets to decrease allergen exposure;
- acid suppression to treat GERD, which may mimic or contribute to EE;
- topical glucocorticoids to decrease esophageal inflammation;
- esophageal dilation to treat strictures.

Dietary therapy is effective for EE in children [85]. It is based upon the observation that patients with EE have a high prevalence of food allergies, and that those allergies may contribute to the development of EE. The appeal of the dietary approach is that it can offer effective non-pharmacological treatment.

Once symptoms are controlled, foods can be reintroduced sequentially. Any foods that result in the worsening of symptoms should be avoided indefinitely [81, 85]. GERD may mimic EE, coexist with it, or contribute to it. Conversely, EE may contribute to GERD [100]. The diagnosis of EE should generally

include demonstration of persistent esophageal eosinophilia at histology after treatment with a PPI (or with a normal pH study).

Most patients with EE respond to topical (*via* a metered-dose inhaler) glucocorticoids, especially with swallowed fluticasone without a spacer [76, 101]. Treatment is generally well-tolerated and patients who are destined to respond tend to do so quickly (within 1 week and often within 1–2 days). Patients frequently relapse if treatment is stopped, and a prevalence of relapse of 14–91% has been reported [102, 103]. Budesonide has been evaluated in case series and randomized trials, and appears to be effective for treating EE [75, 87].

7.4.5 Esophageal Varices

Esophageal varices link the portal and systemic venous circulation. They form as a consequence of portal hypertension, preferentially in the submucosa of the lower esophagus. Hemorrhage from varices is the result of increased pressure within the varix, with a change in the diameter of the varix and an increase in wall tension. Variceal bleeding is associated with a portal vein:hepatic vein gradient >12 mmHg. If the wall tension exceeds the variceal-wall strength, rupture of the varix occurs and therefore hemorrhage results [104]. The literature suggests that >50% of cirrhotic children have varices [104, 105] and that bleeding from varices occurs in 28% of A patients, 30% of B patients, and in 50% of C patients according to the Child–Pugh classification of varices [106].

Endoscopy is the "gold standard" for the diagnosis of esophageal varices because there are no satisfactory non-endoscopic indicators of varices [107]. Therefore, upper GI endoscopy should be done once portal hypertension is suspected or has been diagnosed [108].

Surveillance in adults suggests that in patients without varices upon initial screening endoscopy that endoscopy should be repeated after 3 years, whereas patients with small varices should undergo endoscopy in 1–2 years [109]. Depending on the endoscopic appearance of the varices, a classification according to their shape and size has been proposed [110]:

- F0: no esophageal varices detected;
- F1: small, straight esophageal varices;
- F2: slightly enlarged tortuous esophageal varices occupying less than one-third of the esophageal lumen;
- F3: large, coil-shaped esophageal varices occupying more than one-third of the esophageal lumen.

The management of esophageal varices can be divided into:

- preprimary prophylaxis;
- prophylaxis (primary) of the first episode of bleeding;
- emergency therapy;
- prophylaxis (secondary) of sub¬sequent bleeding episodes.

With regard to management, many data have been extrapolated from adult studies. There are no indications to treat patients to prevent the formation of varices, therefore pre-primary prophylaxis remains an interesting concept that is not applicable in clinical practice.

Prophylaxis of the first episode of bleeding should be carried out with the administration of non-selective beta-blockers (e.g., propranolol) in patients with small varices, whereas endoscopic sclerotherapy and band ligation can be useful in children with medium/large or growing esophageal varices. Of the two endoscopic procedures, band ligation in the pediatric population appears to be superior [104, 107].

The initial management of emergency therapy is stabilization of the patient. Then, intravenous antibiotic therapy (e.g., ceftriaxone) should be part of the treatment of these patients due to the high risk of potentially fatal infectious complications [108]. Endoscopy should be carried within 12–24 h in a stable patient to detect the site of bleeding and to initiate treatment (if indicated).

Endoscopic treatment is very effective in controlling bleeding and consists of sclerother-

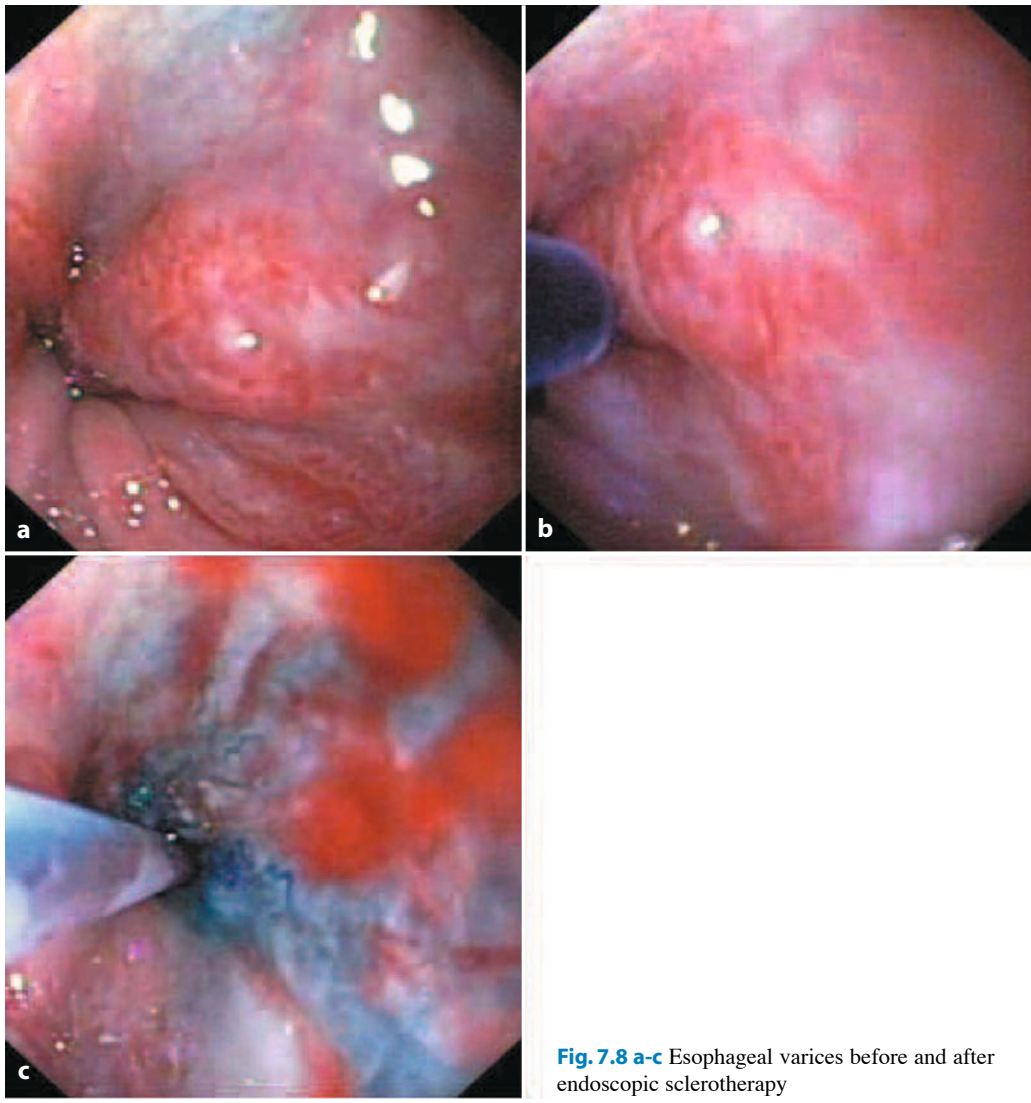

Fig. 7.8 a-c Esophageal varices before and after endoscopic sclerotherapy

apy and variceal ligation. Sclerotherapy requires the injection of agents such as sclerosants or chemically irritating compounds such as ethanolamine/tetradecyl sulfate through the intra- or para-variceal route until bleeding has stopped [104]. Even though sclerotherapy has been used widely in the treatment of esophageal varices in children, recently it has been used less widely because side effects such as perforation, bleeding, ulceration, and stricture formation at the injection site have been reported [108].

Nowadays, endoscopic band ligation (EBL) is recommended for endoscopic therapy. In this technique, a scope loaded with an elastic rubber band is passed through an overtube directly into the varix. After suctioning the bleeding varix into the tip of the endoscope, the rubber band is slipped over the tissue, causing necrosis, ulceration and eventual sloughing of the varix. EBL cannot be conducted in all children because of the size of the esophagus compared with the scope size and the associated ligature attachment, therefore sclerotherapy remains a good alternative (Fig. 7.8).

Secondary prophylaxis should start from day 6 of the bleeding episode. In patients with

cirrhosis, a combination of beta blockers and band ligation is probably the best treatment, but more randomized controlled trials are needed to confirm this finding.

If endoscopic and pharmacological treatment for the prevention of rebleeding is unsuccessful, the transjugular intrahepatic portosystemic shunt (TIPS) should be considered. It should also be considered as a "bridge" to liver transplantation that provides good long-term outcomes in class B/C cirrhosis according to the Child–Pugh classification [107].

7.4.6 Dilation

Esophageal strictures in children may be caused by congenital anomalies, ingestion of caustic agents or foreign bodies, complications of reflux esophagitis, EE, and after esophageal surgery. Such strictures represent a serious challenge for endoscopists.

Various dilators can be used, including "through-the-scope'' balloon dilatation; Savary–Gilliard bougies are the most commonly used in children [111]. The degree of dilation within a session should be based on the severity of the stricture. Initially, the scope is introduced to locate the stricture and (if possible) to pass it to determine its extent and the state of the mucosa. If Savary–Gilliard bougies are used, a guidewire is placed under endoscopic or fluoroscopic control through the stricture, respectively, if the scope can or cannot pass the stricture. The guidewire is then pushed into the stomach. The dilators are then slipped one after the other on the guidewire, thereby achieving longitudinal forces on the stricture [112]. If through-the-scope balloon dilators are used, they are introduced through the accessory canal of an endoscope until they reach the strictures. They are then inflated under fluoroscopic control to reach the desired diameter (Fig. 7.9). Endoscopic control is necessary for Savary–Gilliard or balloon dilators to determine the diameter of the dilated stricture and to ascertain the integrity of the esophagus and possible bleeding sources [111]. The principal complications of esophageal dilation are perforation, bleeding, and aspiration. The risk of perforation is the most dangerous, and is higher in caustic strictures (≤15%) [113].

7.4.7 EUS

There are three basic echo endoscope designs: radial array, curvilinear array, and high-frequency catheter-based mini-probes. The radial system permits circumferential views with angles from 270° to 360° and with frequencies from 5.0 MHz to 10 MHz. The curvilinear scope provides a 180° view that is parallel to the shaft of the echo endoscope, thereby allowing real-time visualization of fine-needle aspiration. Mini-probes pass through the accessory channels of conventional endoscopes and have high resolution but poor penetration. Therefore, they are used to define submucosal lesions or used in luminal strictures which do not permit the passage of conventional echo endoscopes [2].

EUS provides images of the wall of the GI tract that consists of five alternating hyperechoic and hypoechoic layers:

- the innermost layer (lumen) is hyperechoic, and is attributed to the initial echo interface between the ultrasound waves, the mucosa of the GI tract, and surrounding fluid;
- the second layer is a hypoechoic and corresponds to the mucosa and deep mucosa;
- the third layer is a hyperechoic and corresponds to the submucosa;
- the fourth layer represents the muscularis propria and it is hypoechoic;
- the fifth layer, which is seen as a hyperechoic band, is the esophageal serosa.

In the pediatric population, the need for these procedures is far less frequent in children than in adults; this is because of the higher incidence of malignant diseases in adults [9]. However, EUS may have an important diagnostic and therapeutic role in children, particularly in esophageal diseases.

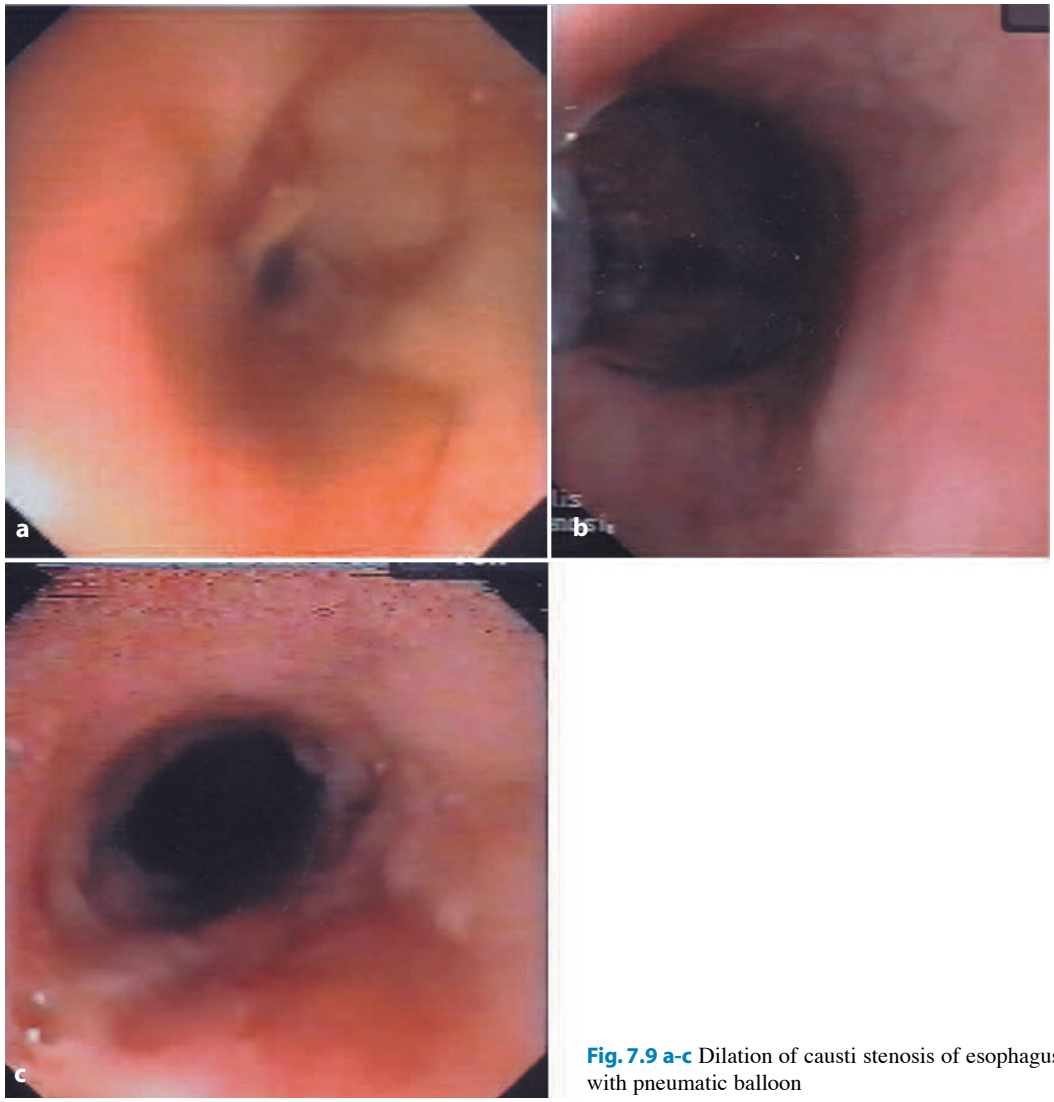

Fig. 7.9 a-c Dilation of causti stenosis of esophagus with pneumatic balloon

EUS can be useful in the differential diagnosis of EE. In fact, in these patients, EUS shows a thickened mucosa in the proximal and distal part of the esophagus compared with controls and in patients with GERD [114, 115]. EUS has been demonstrated to be superior to standard upper GI endoscopy for the identification of esophageal varices. Esophageal varices appear as hypoechoic or anechoic lumens in the esophageal wall, usually in the submucosal layers [108]. Moreover, EUS can more accurately determine the variceal size and the thickness of the variceal wall by measuring the radius of the external and internal wall of the varices [116]. Adult studies have shown that EUS can be used to guide injection sclerotherapy and then to verify the obliteration of varices after endoscopic treatment [117].

EUS can also be used for finding the cause and subsequent treatment strategy for esophageal stenosis in children. This is because EUS can show hyperechoic lesions, suggesting cartilage at the esophageal narrowing or hypertrophy of the muscular layer or hyperechoic rings outside the esophageal wall, indicating that a tracheobronchial remnant is present [118,

119]. In conclusion, EUS is feasible and safe and has a significant impact on the management of pediatric esophageal diseases [120].

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