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Endoscopic Features of Eosinophilic Esophagitis: From Its Origins to Current Practice and Innovations. Literature Review and Personal Experience

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Aim: to systematize literature data and the authors' own findings regarding the endoscopic features of eosinophilic esophagitis.
Key points. Eosinophilic esophagitis is a chronic inflammatory disease of the esophagus characterized by marked eosinophilic infiltration of the esophageal mucosa, as well as subepithelial and submucosal fibrosis. These changes lead to functional impairment of the esophagus, stricture formation, and luminal narrowing, clinically manifesting as progressive dysphagia and episodes of luminal obstruction by a food bolus. Timely diagnosis and appropriate treatment of eosinophilic esophagitis help prevent the development of strictures and other complications.
The diagnosis relies on endoscopic evaluation with the procurement of multiple biopsies (at least six) from the esophageal mucosa to confirm a characteristic histological picture. The main and additional endoscopic findings in eosinophilic esophagitis include edema, linear furrows, rings, exudates, strictures, so-called "feline" esophagus, narrow-caliber esophagus, and the "crepe-paper" esophagus. In recent years, new endoscopic signs have been proposed, such as multiple polypoid lesions, esophageal changes resembling "ankylosaur back" and a "caterpillar track" pattern. Despite the range of possible endoscopic findings, they exhibit relatively low specificity and may be overlooked by endoscopists, leading to delayed diagnosis. High-resolution endoscopic equipment and the development of artificial intelligence programs for image processing hold promise in improving diagnostic accuracy.
Conclusion. Esophagogastroduodenoscopy is the key method for diagnosing eosinophilic esophagitis: awareness of the disease's endoscopic signs and taking multiple biopsies from the esophagus when eosinophilic esophagitis is suspected allow early diagnosis — prior to the onset of complications — thereby enabling timely treatment to prevent stricture formation.
Keywords: eosinophilic esophagitis, esophagogastroduodenoscopy, dysphagia, EREFS scale
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Эндоскопическая семиотика эозинофильного эзофагита: от истоков к современности. Обзор литературы и собственный опыт

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Цель: систематизировать литературные и собственные данные об эндоскопической семиотике эозинофильного эзофагита.
Основные положения. Эозинофильный эзофагит — хроническое воспалительное заболевание пищевода, характеризующееся выраженной эозинофильной инфильтрацией слизистой оболочки пищевода, развитием субэпителиального и подслизистого фиброза, приводящими к нарушению функции пищевода, развитию стриктур и сужению просвета пищевода, что клинически проявляется прогрессирующей дисфагией, эпизодами обтурации пищевода пищевым комком. Своевременная диагностика и адекватное лечение эозинофильного эзофагита позволяют предотвратить развитие стриктур и других осложнений.
Установление диагноза базируется на данных эндоскопического исследования с забором большого числа биоптатов (не менее шести) из слизистой оболочки пищевода с подтверждением характерной гистологической картины. Описаны основные и дополнительные эндоскопические признаки эозинофильного эзофагита, к которым относят отек, борозды, кольца, экссудат, стриктуры, «кошачий» пищевод, пищевод узкого калибра, пищевод по типу «гофрированной бумаги». В последние годы предложены новые эндоскопические симптомы, такие как множественные полиповидные поражения, изменения слизистой оболочки пищевода по типу «спины анкилозавра» и «гусеничного следа». Несмотря на многообразие эндоскопических изменений, они обладают невысокой специфичностью, их могут пропустить врачи-эндоскописты, что приводит к запоздалой диагностике заболевания. Большие надежды возлагаются на использование эндоскопической аппаратуры высокого разрешения, создание программ искусственного интеллекта для обработки эндоскопического изображения.
Заключение. Эзофагогастродуоденоскопия является ключевым методом в диагностике эозинофильного эзофагита: знание эндоскопических признаков заболевания, проведение множественной биопсии из пищевода при подозрении на эозинофильный эзофагит позволит своевременно (еще до развития осложнений) установить диагноз, начать лечение, предотвратить развитие стриктур.
Ключевые слова: эозинофильный эзофагит, эзофагогастродуоденоскопия, дисфагия, шкала EREFS
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Eosinophilic esophagitis (EoE) is a chronic, T2-type immune-mediated inflammatory disease of the esophagus, characterized by a pronounced eosinophilic infiltration of the esophageal mucosa exceeding 15 eosinophils per high-power field (magnification 3400) or more than 60 eosinophils per mm^2, as well as subepithelial and submucosal fibrosis. Clinically, it manifests with swallowing disorders (dysphagia, food impaction and regurgitation etc.) [1–3].

Over the past few decades, there has been a continuous rise in EoE incidence. According to a systematic review and meta-analysis published in 2023, the incidence of EoE currently stands at 5.31 cases per 100,000 individuals annually (95% CI: 3.98–6.63; based on 27 studies with a total sample size of 42,191,506) [4]. EoE predominantly affects males (75 %), mainly children, adolescents, and young adults [1, 5, 6].

Current models of EoE progression describe a gradual transition from inflammatory changes to fibrosis and esophageal stenosis, with the majority of patients eventually developing dysphagia. One retrospective study demonstrated that a 20-year delay in diagnosis and treatment resulted in 87.5 % of patients having fibrose changes in the esophageal wall and 70.8 % exhibiting strictures [7]. In contrast, timely diagnosis and the initiation of pharmacological therapy in the early stages can slow the progression of disease and prevent stricture formation and other complications of EoE [7, 8].

Diagnosis of EoE is based on the combined assessment of clinical symptoms (dysphagia, substernal pain, episodes of food impaction, heartburn, etc.), esophagogastroduodenoscopy (EGDS) findings, and histopathological examination of esophageal biopsies (eosinophilic infiltration of the esophageal mucosa, subepithelial fibrosis). Because early-stage EoE often presents with nonspecific symptoms (heartburn, odynophagia, epigastric pain, nausea) that can be seen in many other conditions, the cornerstone of prompt diagnosis is an EGD with properly conducted biopsy sampling (Fig. 1) [1].

During esophagoscopy, the majority (85–90 %) of patients with eosinophilic esophagitis display nonspecific signs of active inflammation and the consequences of its prolonged persistence [6, 9]. Approximately 10–15 % of EoE patients, however, show no visible changes in the esophageal lumen or mucosa on EGD [10, 11].

A 2012 meta-analysis encompassing 4,678 patients with eosinophilic esophagitis and 2,742 controls (without EoE) demonstrated moderate sensitivity and moderate negative and positive

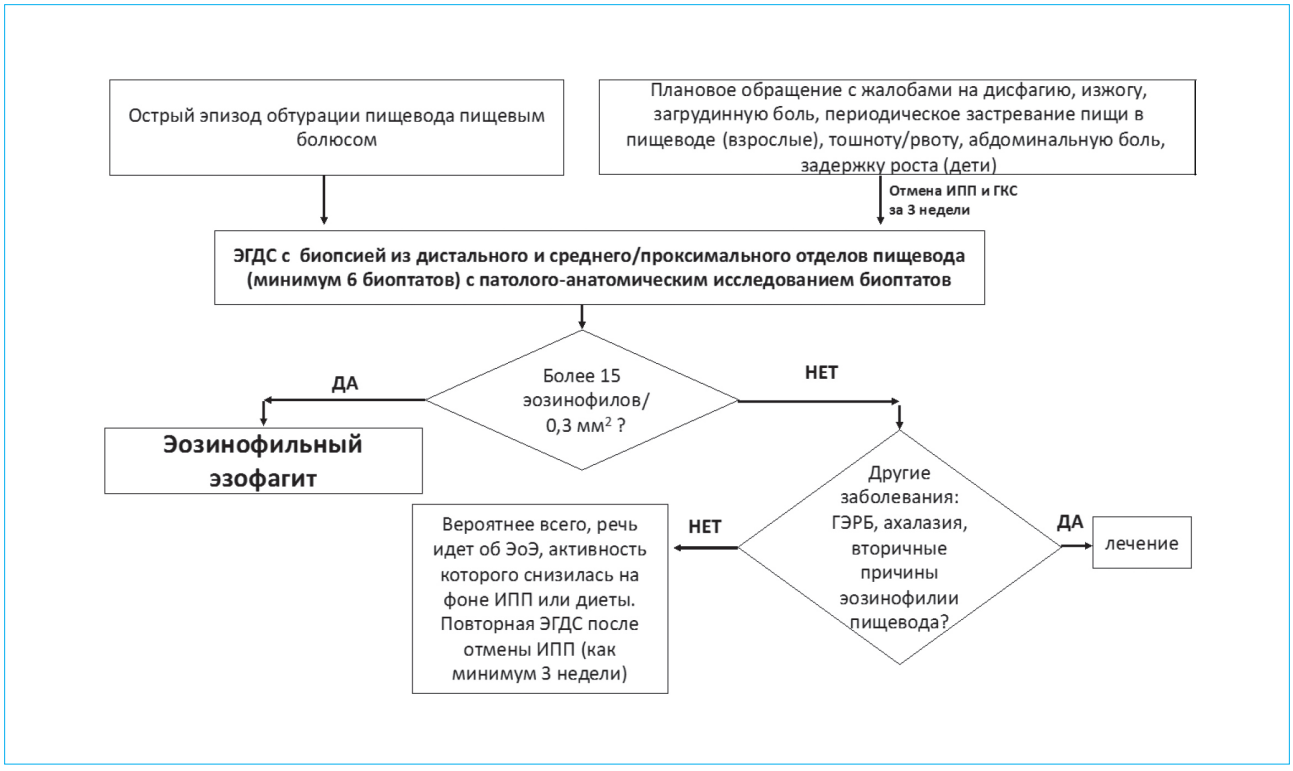


Figure 1. Diagnostic algorithm for eosinophilic esophagitis (according to [1] with alterations)

Рисунок 1. Алгоритм диагностики эозинофильного эзофагита (по [1] с изменениями)

predictive values of various endoscopic findings for establishing the EoE diagnosis [12].

Modern high-resolution video endoscopy with multimodal image enhancement and magnification significantly increases the diagnostic yield of endoscopic assessments, facilitating correct diagnosis of EoE in up to 95 % of cases. Endocytoscopy, using magnification up to 310, allows for microscopic visualization of intraepithelial eosinophils characterized by bilobed nuclei during esophagoscopy [13, 14].

Another major leap forward in detecting this condition is the use of clinical decision support systems ("artificial intelligence"), which can differentiate eosinophilic esophagitis from a normal esophagus with an accuracy exceeding 95 %, outperforming the endoscopist in this regard [15, 16].

In a seminal paper by I. Hirano et al. (2013) on the systematic endoscopic evaluation of EoE findings, the principal (major) and secondary endoscopic features of eosinophilic esophagitis were first delineated and ranked (Table 1) [17].

After collegial validation by participating endoscopists, the major (key) features of eosinophilic esophagitis include fixed (non-distensible) rings, exudates, longitudinal furrows, edema, and strictures, and a corresponding rating scale has been proposed (Fig. 3–7) [17].

Major/Key Endoscopic Features of eosinophilic esophagitis

1. *Fixed (non-distensible) rings (synonyms: concentric rings; trachealization of the esophagus, i.e. a structural change resembling the trachea)* (Fig. 2): circular structures of the esophageal wall, typically multiple. Like strictures, rings result from esophageal remodeling due to subepithelial fibrosis, and their presence correlates with an increased risk of food impaction because of decreased esophageal distensibility [18].

The severity of rings does not correlate with the degree of mucosal eosinophilic infiltration; it tends to persist despite treatment — even after improvement in the histologic profile [19, 20]. It is known that rings may be detected in about 10 % of patients with esophagitis of other etiologies, including gastroesophageal reflux disease (GERD) [21, 22]. At the third (most severe) grade of ring formation, rings prevent the passage of an 8–9.5 mm diagnostic endoscope. From this perspective, they very closely approximate what is termed an "esophageal stricture". However, because an endoscopically impassable narrowing of the esophageal lumen is not always caused by fixed rings — sometimes it is due to an extended narrowing commonly referred to as a "narrow-caliber

Table 1. Original classification and grading system for the endoscopic assessment of the esophageal features of eosinophilic esophagitis [17]

Таблица 1. Классификация и оценочная шкала признаков эозинофильного эзофагита [17]

Major features ***Главные/основные признаки***	
Fixed rings (also referred to as concentric rings, corrugated oesophagus, corrugated rings, ringed oesophagus, trachealisation) ***Фиксированные (нерасправляющиеся) кольца*** *(также называемые концентрическими кольцами, гофрированным пищеводом, гофрированными кольцами, кольчатым пищеводом, трахеализацией)*	
Grade ***Степень***	**Description** ***Описание***
0	Absent *Отсутствуют*
1	Mild (subtle circumferential ridges) *Легкая (негрубые, слегка заметные кольцевидные выступы)*
2	Moderate (distinct rings that do not impair the passage of a standard diagnostic adult endoscope with outer diameter 8–9.5 mm) *Умеренная (кольца, не препятствующие проведению стандартного взрослого диагностического эндоскопа диаметром 8–9,5 мм)*
3	Severe (distinct rings that do not permit the passage of a diagnostic endoscope) *Тяжелая (отчетливо выраженные кольца, препятствующие проведению диагностического эндоскопа)*
Exudates (also referred to as white spots, plaques) ***Экссудат*** (также называемые белыми пятнышками, бляшками)	
0	Absent *Отсутствуют*
1	Mild (lesions involving < 10 % of the esophageal surface area) *Легкая (экссудат, покрывающий < 10 % поверхности пищевода)*
2	Severe (lesions involving ≥ 10 % of the esophageal surface area) *Тяжелая (экссудат, покрывающий ≥ 10 % поверхности пищевода)*
Furrows (also referred to as vertical lines, longitudinal furrows) ***Борозды*** *(синонимы: вертикальные линии, продольные борозды)*	
0	Absent *Отсутствуют*
1	Mild (vertical lines without visible depth) *Легкая (имеются вертикальные линии без видимого углубления)*
2	Severe (vertical lines with mucosal depth) *Тяжелая (вертикальные линии с углублением/вдавлением в слизистой оболочке)*
Oedema (also referred to as decreased vascular pattern, mucosal pallor) ***Отек*** *(оценивается по снижению четкости, обеднению или отсутствию сосудистого рисунка и бледности слизистой оболочки)*	
0	Absent *Отсутствует (сосудистый рисунок четкий)*
1	Mild (reduced vascularity or loss of clarity of vascular markings) *Легкая (снижение четкости сосудистого рисунка)*
2	Severe (absence of vascular markings) *Тяжелая (отсутствие сосудистого рисунка)*
Stricture ***Стриктура***	
0	Absent *Отсутствуют*
1	Present *Имеется*
Minor features ***Второстепенные признаки***	
Feline esophagus (transient, concentric mucosal rings observed spontaneously or during belching, retching or swallowing that disappear with air insufflation) ***«Кошачий» пищевод*** *(временно появляющиеся концентрические кольца слизистой оболочки пищевода, наблюдаемые спонтанно или во время отрыжки, рвотных позывов или глотания, которые исчезают при инсуффляции воздуха)*	

End of Table 1. Original classification and grading system for the endoscopic assessment of the esophageal features of eosinophilic esophagitis [17]

Окончание таблицы 1. Классификация и оценочная шкала признаков эозинофильного эзофагита [17]

0	Absent *Отсутствуют*
1	Present *Имеется*
Narrow-caliber esophagus (reduced luminal diameter of the majority of the tubular esophagus) ***Пищевод узкого калибра*** *(уменьшенный диаметр просвета большей части трубчатого пищевода)*	
0	Absent *Отсутствуют*
1	Present *Имеется*
Crepe paper esophagus (mucosal fragility or laceration upon passage of diagnostic endoscope but not after esophageal dilation) ***Пищевод, напоминающий креп-бумагу*** *(характерна ранимость и надрывы слизистой оболочки при проведении диагностического эндоскопа по пищеводу, но не в результате выполнения его дилатации)*	
0	Absent *Отсутствуют*
1	Present *Имеется*

esophagus" — "stricture" is listed as a separate item among the major features.

2. *Exudates on the esophageal mucosa (synonyms: white plaques, white coating, white deposits)*. A whitish exudate (Fig. 3) represents nothing other than eosinophilic microabscesses [23]. When the endoscopic features of EoE are not well known, this exudate is often mistaken for Candida esophagitis.

3. *Furrows in the esophageal mucosa, also described as vertical lines or longitudinal furrows*, indeed appear as shallow linear depressions in the esophageal lining running along the esophageal axis (Fig. 4). Furrows can be recognized more easily by reducing luminal distension (aspirating the introduced air) or by using indigo carmine chromoendoscopy. Blood that enters these furrows — for instance, after biopsy — can also aid in highlighting them. It is worth noting that, in both origin and appearance, furrows differ from erosive epithelial lesions seen in GERD, though both can be observed simultaneously in the same patient.

4. *Oedema of the esophageal mucosa* (Fig. 5) is evaluated based on diminished clarity, reduced

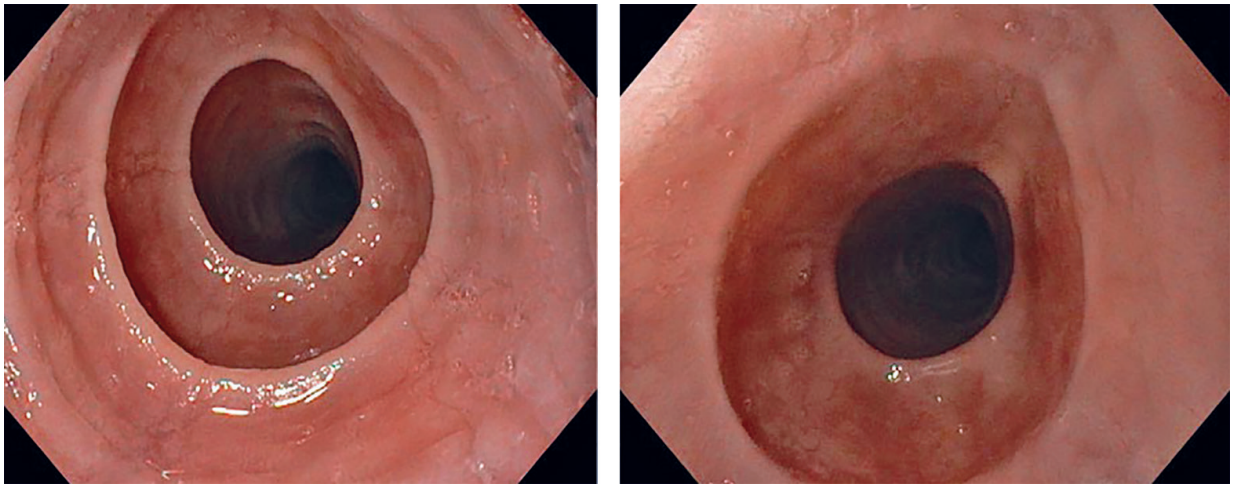
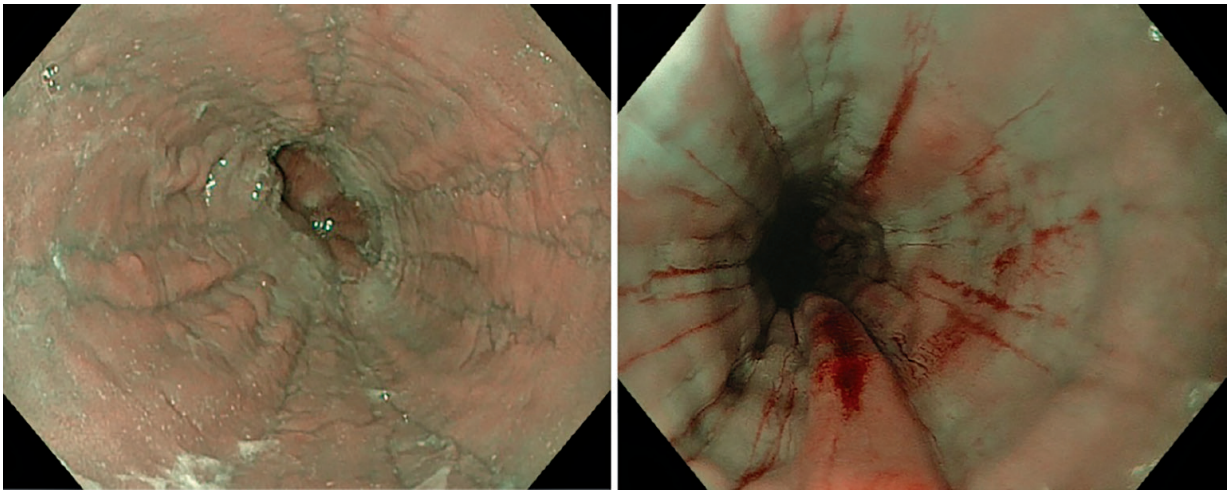


Figure 2. Endoscopic picture of fixed rings in the patient with eosinophilic esophagitis

Рисунок 2. Эндофотография. Фиксированные (нерасправляющиеся) кольца стенки пищевода при эозинофильном эзофагите

Figure 3. Endoscopic picture of exudates in the patient with eosinophilic esophagitis

Рисунок 3. Эндофотография. Экссудат слизистой оболочки пищевода при эозинофильном эзофагите



A B

Figure 4. Endoscopic picture of furrows in the patient with eosinophilic esophagitis: A — in narrow band imaging; B — the visibility of furrows is enhanced after esophageal biopsies with blood pouring on the furrows

Рисунок 4. Эндофотография. Борозды слизистой оболочки пищевода при эозинофильном эзофагите: А — борозды хорошо видны при осмотре в узкоспектральном режиме, т.е. в сине-зеленом свете; В — борозды подчеркнуты за счет контрастирования кровью после проведения биопсии

or absent vascular markings, and mucosal pallor. Edema is a relatively nonspecific feature observed in many other esophageal diseases, including GERD, and is considered less diagnostically reliable on endoscopy compared with other findings [24].

5. *Esophageal stricture* (Fig. 6) is diagnosed by the presence of luminal narrowing that prevents the passage of a standard diagnostic adult endoscope (8–9.5 mm in diameter). Unlike GERD-related strictures, EoE strictures may form in the distal, mid, or proximal esophagus [7]. In clinical practice, the appearance of a stricture typically denotes a narrow or small-caliber esophagus.

Minor endoscopic features of eosinophilic esophagitis

In addition to the five key/major endoscopic features described above, other findings frequently encountered during esophagoscopy in patients with eosinophilic esophagitis have been reported. I. Hirano et al. [17] identified three such features:

– *feline esophagus* (Fig. 7): refers to transient, multiple superficial concentric contractions of the muscularis mucosa of the esophagus, resembling ripples on water surface during a gust of wind (synonym: transient mucosal folds). This phenomenon is how the esophagus appears in normal cats (Fig. 7A). Unlike “fixed rings”, these contractions

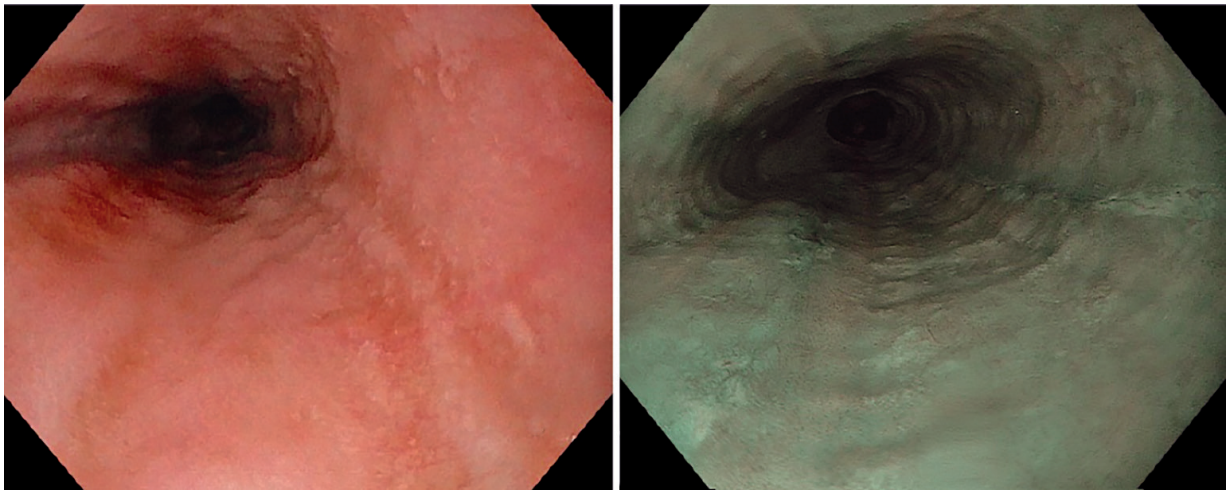


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Figure 5. Endoscopic picture of edema in the patient with eosinophilic esophagitis: A — in white light imaging; B — in narrow band imaging

Рисунок 5. Эндофотография. Отек слизистой оболочки пищевода при эозинофильном эзофагите: A — в белом свете; B — в узкоспектральном режиме

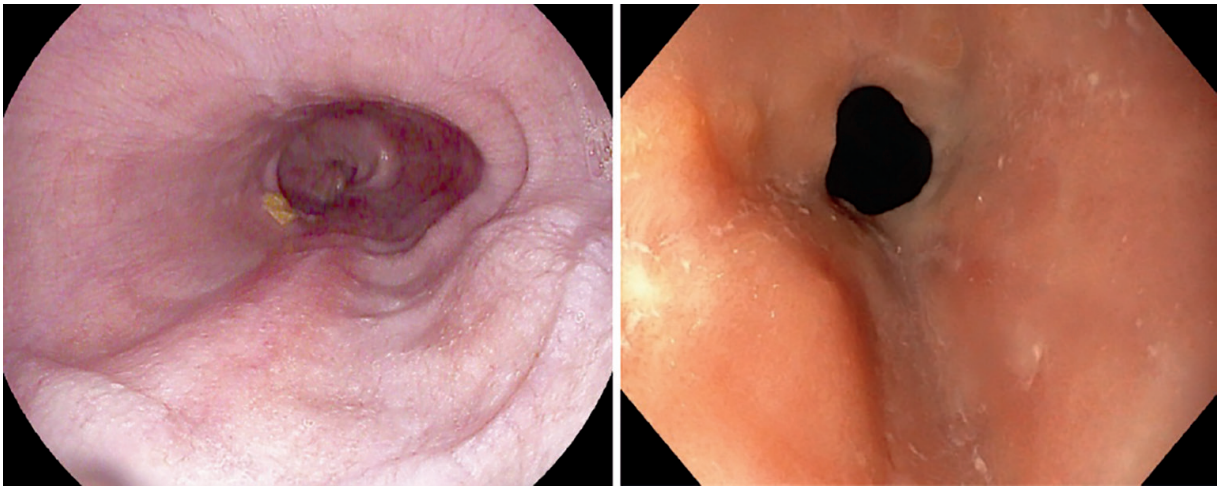
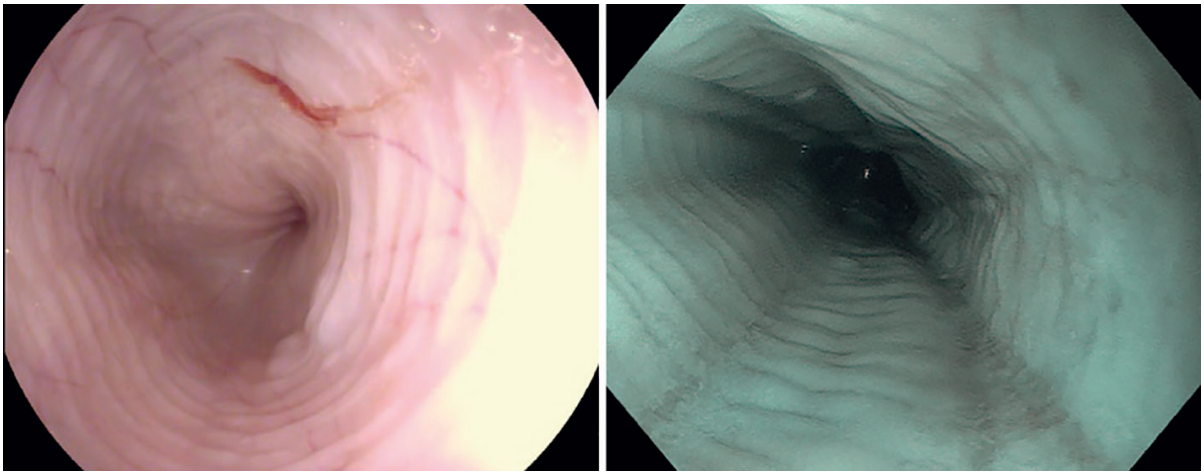


Figure 6. Endoscopic picture of strictures in the patient with eosinophilic esophagitis

Рисунок 6. Эндофотография. Стриктуры пищевода при эозинофильном эзофагите

appear spontaneously or during belching, retching, or swallowing and completely disappear once air is insufflated. This distinctive characteristic helps avoid confusing a “feline esophagus” with esophageal trachealization. The term “feline esophagus” most often describes thin, delicate contractile rings periodically noted on endoscopy in situations unrelated to eosinophilic esophagitis, including in normal esophagi [17].

— *narrow-caliber esophagus* (synonym: small-caliber esophagus): defined as a diffuse decrease in the luminal diameter along most of the tubular esophagus, differing from GERD-related strictures or anastomotic strictures after surgery (Fig. 8), which typically manifest as shorter, localized narrowing, along with proximal dilation above the stricture. In advanced stages, a narrow-caliber esophagus may impede passage of a



A B

Figure 7. "Feline" oesophagus. A — endoscopic picture of a cat's esophagus in white light imaging (provided by A.S. Shatalov); B — endoscopic picture of "feline" esophagus in the patient with eosinophilic esophagitis in narrow band imaging

Рисунок 7. «Кошачий» пищевод. А — эндофотография пищевода кошки в белом свете (предоставлена А.С. Шаталовым); В — эндофотография «кошачьего» пищевода у пациента с эозинофильным эзофагитом в узкоспектральном режиме

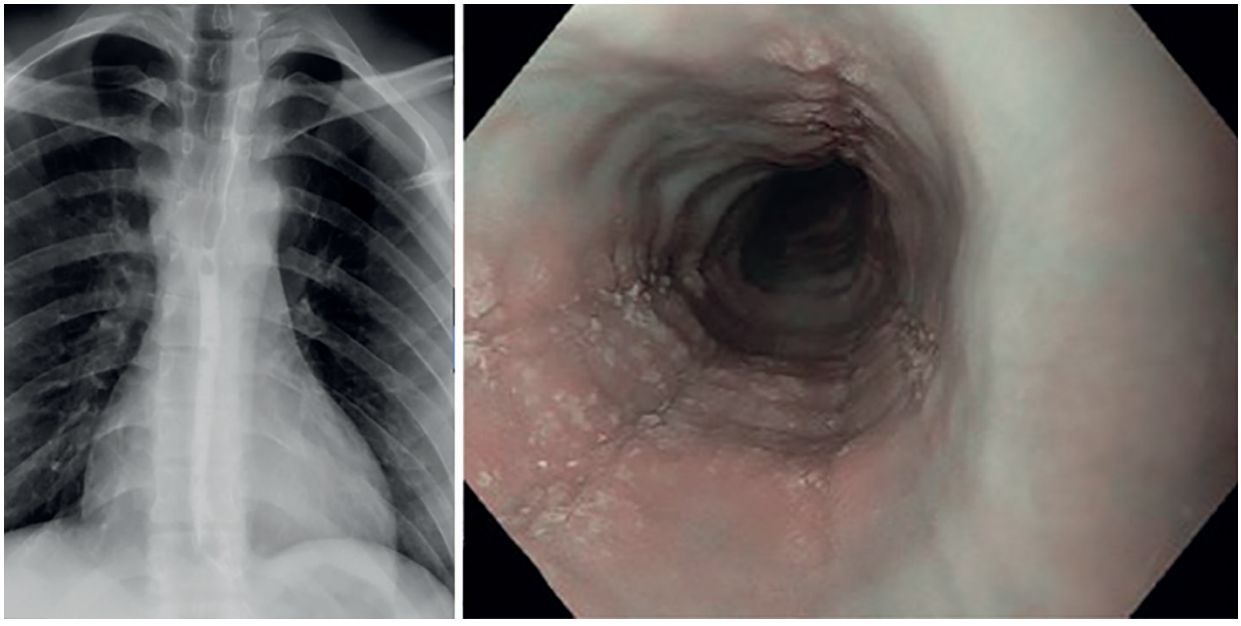


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Figure 8. Narrow-caliber esophagus: A — barium esophagogram shows narrow-caliber esophagus from the upper to lower esophagus in the patient with eosinophilic esophagitis; B — endoscopic picture of narrow-caliber esophagus in the same patient

Рисунок 8. Узкокалиберный пищевод: А — рентгеноскопия с контрастом, сужение просвета большей части трубчатого пищевода при эозинофильном эзофагите; В — эндофотография пищевода того же пациента

diagnostic endoscope. Interestingly, although both "rings" and "strictures" are classified as major endoscopic features of EoE, a luminal diameter reduction affecting most of the tubular esophagus is not.

D.A. Carlson and I. Hirano proposed a provisional definition of a "narrow-caliber esophagus" as one in which more than 50 % of the esophagus measures under 18 mm in luminal diameter [25]. The sensitivity of esophagoscopy for detecting a luminal diameter below 18 mm, as documented by radiologic studies, is only about 25 %, i.e. quite low [26]. A barium swallow is more successful than endoscopy at identifying the luminal narrowing characteristic of a narrow-caliber esophagus [27, 28].

Clinically, even when not at its most severe stage, a narrow-caliber esophagus often underlies acute-onset dysphagia caused by an impacted foreign body — generally a large, inadequately chewed piece of meat [29]. It is no coincidence that eosinophilic esophagitis has sometimes been referred to as "shashlik syndrome" or the "steakhouse syndrome". Following successful removal of the impacted material and restoration of luminal patency, endoscopists, finding no obvious isolated stricture and perhaps overlooking other EoE-related lesions in this emergency context, fail to perform biopsies in 40 % of patients [30]. Quite often (in 22 %–55 % of cases), patients are discharged without undergoing a repeat esophagoscopy or biopsy (24–72 % of cases), leaving them without a definitive diagnosis or timely and appropriate treatment [31].

— *crepe paper esophagus* (Fig. 9): the esophageal mucosa resembles this particular type of paper, showing characteristic fragility and tearing even with minimal contact from a diagnostic endoscope as it passes through the organ. Similar changes that arise as a consequence of esophageal dilation should not be regarded as manifestations of the "crepe paper" sign. While not very common, the crepe paper esophagus is a pathognomonic indicator of eosinophilic esophagitis, retained in the group of minor (secondary) signs.

To enhance the diagnostic yield of esophagoscopy for EoE, as well as to standardize the assessment of the presence, nature, and severity of esophageal changes, I. Hirano et al. [17] conducted a meticulous validation of their original classification system and rating scale (Table 2) for the endoscopic features of eosinophilic esophagitis.

Following this work, the group developed and proposed a modified classification and rating scale for EoE-related findings at endoscopy.

After introducing several minor revisions to I. Hirano's scale — such as removing secondary features from the classification, reordering the major features, and changing the English term "Oedema" to "Edema" — the classification ultimately became known as "EREFS", an acronym derived from the five major endoscopic features of eosinophilic esophagitis it includes (Edema, Rings, Exudates, Furrows, Strictures). Since both "Edema" and "Exudates" begin with "E," some propose "ERExFS" as a potentially more distinguishable variant.

The EREFS classification was validated in adults in a prospective multicenter study that demonstrated strong interobserver agreement between clinicians in clinical practice and those in academic settings [19, 32]. External validation of the EREFS scale showed consistent assessment of

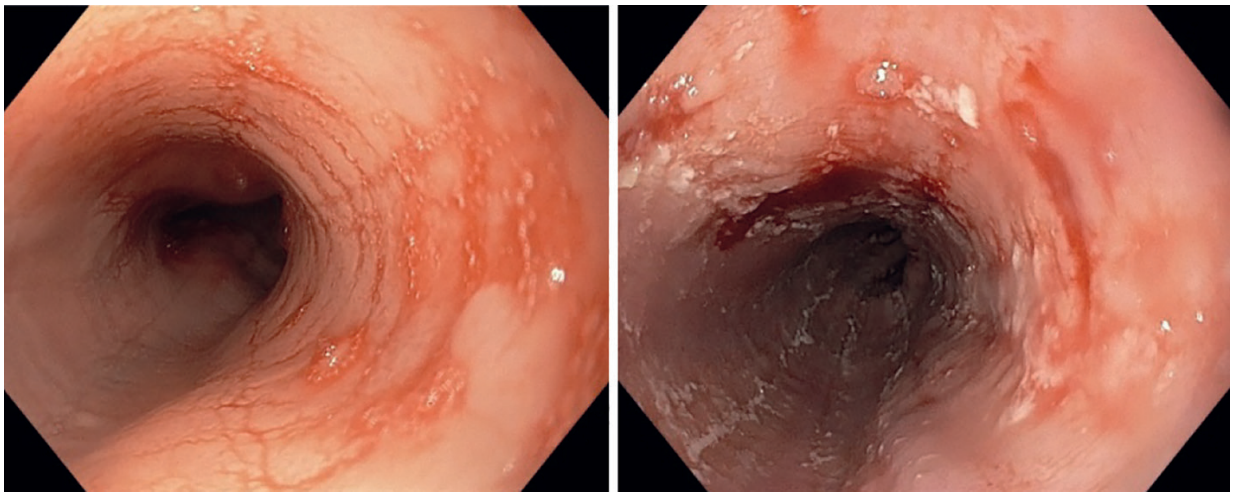


Figure 9. Endoscopic picture showing fragility and ruptures of the esophageal mucosa in eosinophilic esophagitis
Рисунок 9. Эндофотография. Ранимость и надрывы слизистой оболочки пищевода при эозинофильном эзофагите

Table 2. The eosinophilic esophagitis endoscopic reference score (EREFS)
Таблица 2. Классификация и оценочные шкалы эозинофильного эзофагита (EREFS)

Endoscopic findings *Эндоскопические признаки*	Grade *Степень*	Hirano et al., 2013	van Rhijn et al., 2016	Ma et al., 2022
Отек ***Edema***	Absent (distinct vascularity is present) *Отсутствует (сосудистый рисунок четкий)*	0	0	0
	Mild (reduced vascularity or loss of clarity of vascular markings) *Легкая (обеднение или снижение четкости сосудистого рисунка)*	1		1
	Severe (absence of vascular markings) *Тяжелая (отсутствие сосудистого рисунка)*		1	2
Кольца ***Rings***	Absent *Отсутствуют*	0	0	0
	Mild (subtle circumferential ridges) *Легкая (негрубые кольцевидные выступы)*	1	1	1
	Moderate (distinct rings that do not impair the passage of a standard diagnostic adult endoscope with outer diameter 8–9.5 mm) *Умеренная (отчетливо выраженные кольца, не препятствующие проведению стандартного взрослого диагностического эндоскопа диаметром 8–9,5 мм)*	2	2	2
	Severe (distinct rings that do not permit the passage of a diagnostic endoscope) *Тяжелая (отчетливо выраженные кольца, препятствующие проведению диагностического эндоскопа)*	3	3	3
Экссудат ***Exudates***	Absent *Отсутствует*	0	0	0
	Mild (lesions involving < 10 % of the esophageal surface area) *Легкая (экссудат, покрывающий менее 10 % поверхности пищевода)*	1	1	1
	Moderate (lesions involving > 10 % and < 25 % of the esophageal surface area) *Средняя (экссудат, покрывающий ≥ 10 % и < 25 % поверхности пищевода)*	2		2
	Severe (lesions involving ≥ 25 % of the esophageal surface area) *Тяжелая (экссудат, покрывающий ≥ 25 % поверхности пищевода)*			3
Борозды ***Furrows***	Absent *Отсутствует*	0	0	0
	Mild (vertical lines present without visible depth) *Легкая (имеются вертикальные линии без видимого углубления)*	1	1	1
	Severe (vertical lines present with mucosal depth) *Тяжелая (вертикальные линии с углублением/вдавлением в слизистой оболочке)*			2
Стриктура ***Stricture***	Absent *Отсутствует*	0	0	0
	Present *Имеется*	1	1	1

eosinophilic esophagitis features between experienced and novice endoscopists [33].

Efforts to find an optimal grading scheme for the main EoE features are ongoing, given the relative "youth" of this disease entity and a desire for ever more detailed stratification of its key signs [34]. The original EREFS (I. Hirano et al., 2013 [17]), a simplified EREFS (B.D. van Rhijn et al., 2016 [20]), and a maximally expanded EREFS (C. Ma et al., 2022 [34]) each assign scores from 0 to 8, 0 to 7, and 0 to 11, respectively (Table 2).

The EREFS scale can be used to evaluate the overall severity of endoscopic changes at diagnosis, during treatment, or when titrating maintenance doses of medications or diet, based on the total point score. The point tally can be calculated either by considering all five features (for example, E1R1Ex2F1S0 = 5 points) or by separately scoring the inflammatory parameters (edema, exudates, and longitudinal furrows) — e.g., E2Ex1F2 = 5 points — and the fibrotic parameters (rings and strictures) — e.g., R2S1 = 3 points.

An optimal cutoff value for the total EREFS score to confirm a diagnosis of eosinophilic esophagitis has not been definitively established. Some authors have demonstrated that EREFS > 2 may indicate EoE with relatively high sensitivity and specificity [35], whereas others have argued that this threshold is insufficient to distinguish between eosinophilic and noneosinophilic esophagitis because of low specificity despite high sensitivity [36]. This discrepancy may be attributable to varying degrees of EoE-related endoscopic abnormalities across different patient cohorts, as well as the clinical profiles of comparison groups comprising patients with noneosinophilic esophagitis.

Notably, endoscopic disease activity measured by the EREFS scale does not always correlate with clinical symptoms or histologic activity of the disease [37, 38]. Nonetheless, a reduction in EREFS scores during therapy can indicate treatment efficacy. When the distribution and degree of endoscopic changes vary within different segments of the esophagus, it is important to base the EREFS assessment on the most severe findings observed [39].

New endoscopic signs of eosinophilic esophagitis

In recent years, several novel endoscopic signs of EoE have been identified:

– *multiple polypoid lesions* [40, 41] (Fig. 10): small, multiple lesions that endoscopically resemble papillomas or glycogenic acanthosis. However, histopathological evaluation does not meet the criteria for either of these diagnoses. Their etiology and clinical significance remain unknown. One might hypothesize that they are somewhat analogous to pseudopolyps in the colon of patients with ulcerative colitis in remission.

– *caterpillar sign* (Fig. 11): this phenomenon resembles the tracks left by tractor treads on the ground, appearing as small concentric ridges on the esophageal mucosa arranged perpendicular to the longitudinal furrows [36, 42].

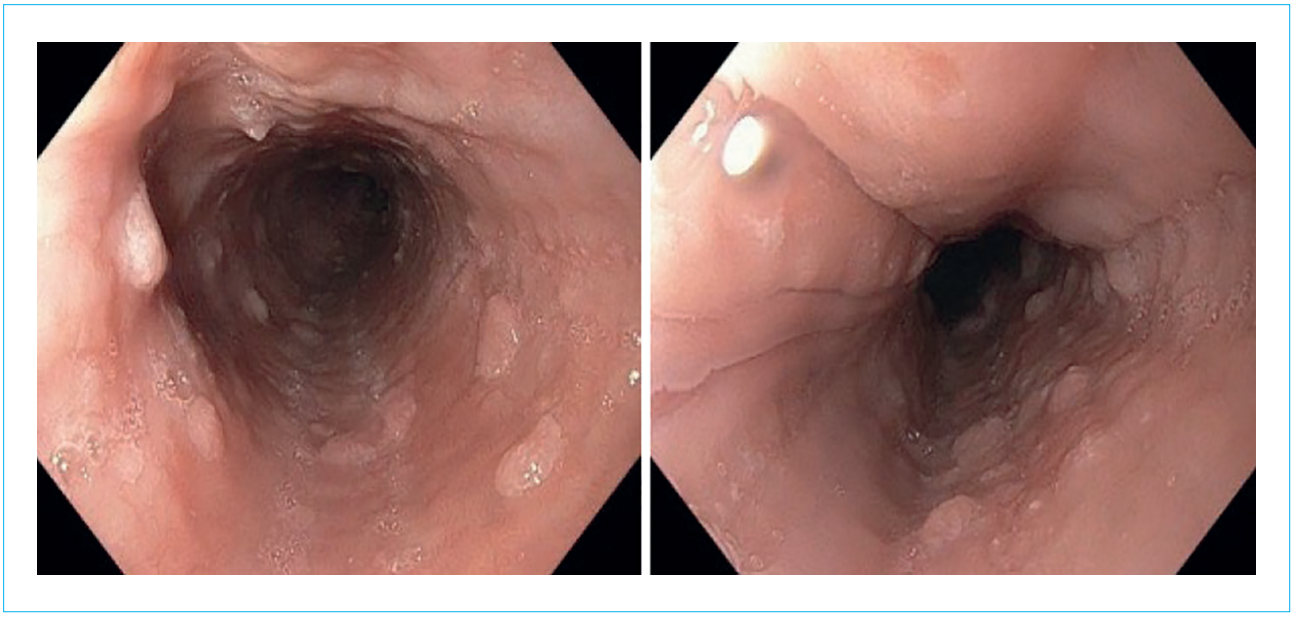


Figure 10. Endoscopic picture of multiple polypoid lesions in the patient with eosinophilic esophagitis (endophotographs provided by R.O. Kuvaev)

Рисунок 10. Эндофотография. Множественные полиповидные поражения пищевода при эозинофильном эзофагите (эндофотографии предоставлены Р.О. Куваевым)

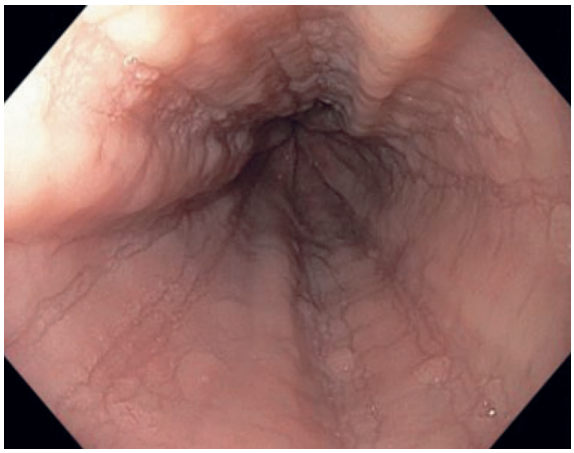


Figure 11. Changes in the surface of the "caterpillar track" type

Рисунок 11. Изменения поверхности по типу «гусеничного следа»

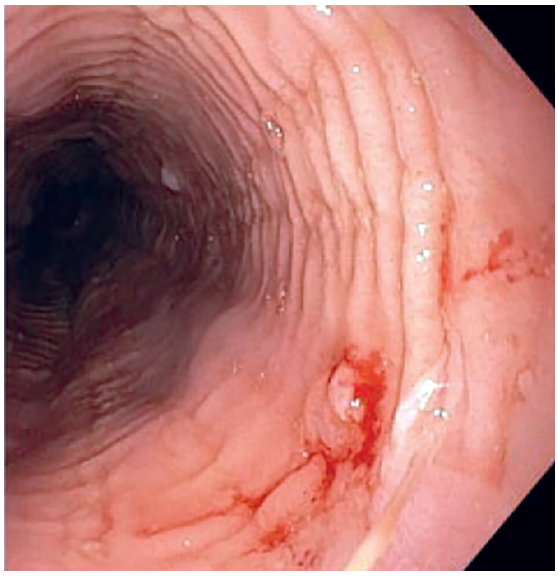
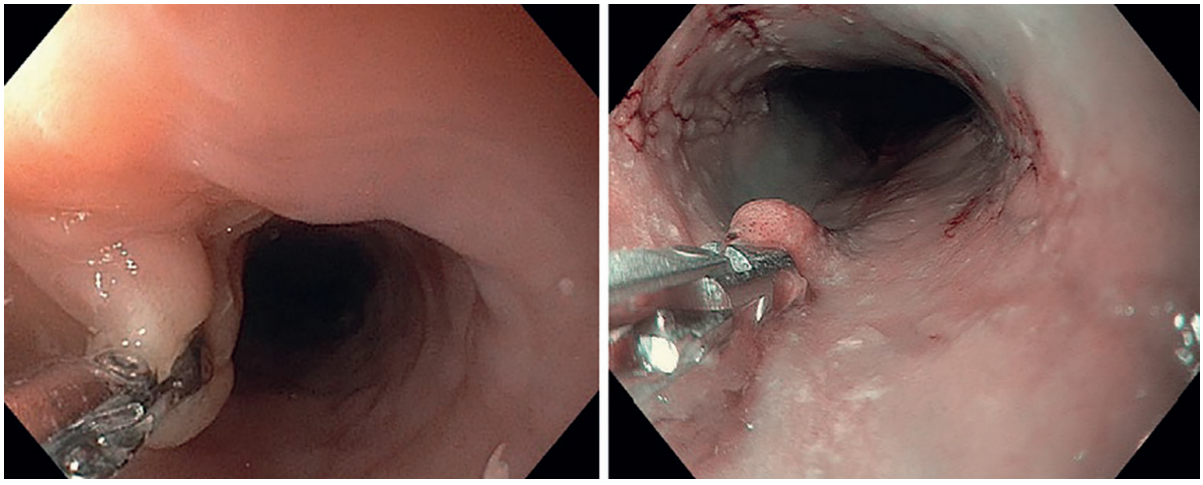


Figure 12. Endoscopic picture of the esophagus: changes in the surface of the esophageal mucosa according to the "ankylosaur back" type in eosinophilic esophagitis

Рисунок 12. Эндофотография пищевода: изменения поверхности слизистой оболочки пищевода по типу «спины анкилозавра» при эозинофильном эзофагите

— *ankylosaurus back sign* [43] (Fig. 12): characterized by multiple small nodular protrusions running longitudinally along the crests of the esophageal mucosal folds. Endoscopically, it recalls the back of an ankylosaurus, a prehistoric dinosaur. Such changes occur more frequently in patients who have coexisting eosinophilic esophagitis and pathological gastroesophageal reflux and may predict a positive response to proton pump inhibitor therapy (attaining histologic remission under acid-suppressive treatment).

— *tug sign / pull sign* [44, 45] (Fig. 13): describes a greater-than-expected resistance (tissue "pull") of the mucosa during biopsy — another



A B

Figure 13. Endoscopic picture of tug sign in the patient with eosinophilic esophagitis: A — in white light imaging; B — in narrow band imaging

Рисунок 13. Эндофотографии, демонстрирующие «признак натяжения» у пациентов с эозинофильным эзофагитом: А — в белом свете; В — в режиме узкого спектра света

feature suggestive of eosinophilic esophagitis. This "tug" or "pull" phenomenon reflects the presence of subepithelial fibrosis. It is observed more often in patients who respond to proton pump inhibitor therapy than in those who do not.

Unfortunately, the aforementioned endoscopic features are not exclusively specific to eosinophilic esophagitis; they also occur in other esophageal diseases. Furthermore, their prevalence, severity, and distribution within the esophagus vary widely. For instance, endoscopically visible lesions may be confined to small segments of the distal esophagus or distributed unevenly along its length in 30–40 % of patients [46, 47]. Such localized changes can be missed if the entire esophagus is not carefully inspected at varying degrees of insufflation and wall distension.

When interpreting endoscopic findings, differential diagnosis most commonly involves esophageal candidiasis and GERD, both of which can also occur concomitantly with eosinophilic esophagitis in the same patient. As regards the diagnostic and monitoring accuracy of the EREFS system, two recent single-center studies have shown conflicting results, indicating that endoscopists should not rely exclusively on endoscopy findings to diagnose EoE or to determine whether the disease is active or in remission.

Endoscopy alone cannot serve as the sole criterion for establishing a diagnosis of eosinophilic esophagitis without histopathological examination of esophageal biopsy specimens. Ultimately, EoE is diagnosed based on clinical symptoms, histologically confirmed esophageal eosinophilia of at least 15 eosinophils per high-power field (approximately 60 eosinophils/mm^2), and exclusion of other disorders and conditions causing secondary esophageal eosinophilia, such as hyper-eosinophilic syndrome, drug-induced esophagitis, achalasia, etc. [48].

According to current consensus documents, forceps biopsy is mandatory in all patients suspected of having EoE on EGD. Separate biopsies from the proximal and distal esophageal mucosa are advised. At least six biopsies should be obtained, and for maximal diagnostic yield, six to eight biopsy samples can be taken from the distal, mid, and proximal esophagus. Biopsy sampling should target areas of typical changes — primarily exudates and longitudinal furrows — because these regions are associated with higher eosinophil counts [1, 48, 49].

Specimens must include full-thickness epithelium and lamina propria to enable assessment of subepithelial fibrosis.

It is also essential to obtain biopsies from both endoscopically abnormal and normal-appearing areas of the mucosa because significant histological changes may be present even where the macroscopic view is unremarkable. At the time of initial endoscopic evaluation, it is prudent to obtain gastric biopsies to rule out eosinophilic gastroenteritis and to determine whether the patient is infected with *H. pylori* [1–3, 6, 48].

Indications for esophageal biopsies [1–3]:

1) an endoscopy suggestive of eosinophilic esophagitis;

2) dysphagia and food impaction in the esophagus, even if endoscopy appears normal;

3) GERD-like symptoms (heartburn, substernal pain, regurgitation) in children that are refractory to PPI therapy, even with a normal endoscopic appearance;

4) an episode of acute food impaction in the esophagus, following endoscopic removal of the impacted food bolus or spontaneous resolution of the obstruction.

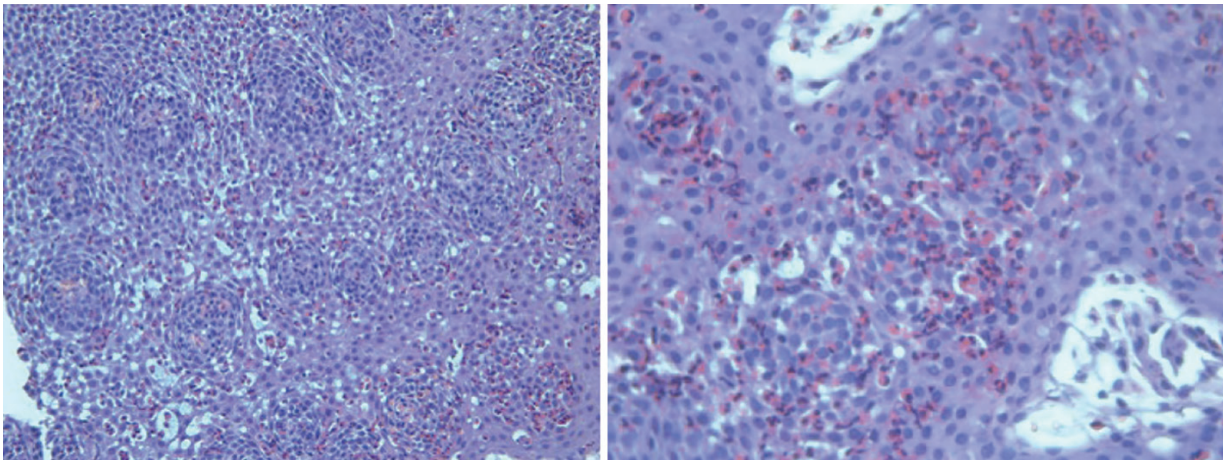
It should be emphasized that the endoscopic appearance is normal in 10–25 % of EoE patients. Therefore, biopsy must be performed in patients with dysphagia even in the absence of visible mucosal changes on endoscopic examination.

It is important to remember that, whenever the patient's condition allows, PPIs and steroids should be discontinued for at least 3 weeks prior to a diagnostic EGD with biopsies to avoid false-negative histologic findings. In patients on acid-suppressive drugs or steroids, the eosinophil count may rise only slightly or remain within normal limits (5 eosinophils per high-power field) [1, 2, 50].

The principal criterion for diagnosing EoE is intraepithelial eosinophilic infiltration with at least 15 eosinophils per high-power field (or ≥ 60 eosinophils per mm^2) (Fig. 14) [1, 2].

Significant intraepithelial eosinophilic infiltration leads to the formation of eosinophilic abscesses, defined as clusters of four or more eosinophils in dilated intercellular spaces, and the accumulation of eosinophils on the mucosal surface. These changes are typically associated with damage to the superficial layer of the stratified squamous epithelium. Characteristic findings also include interstitial edema, papillary elongation in the squamous epithelium, basal cell hyperplasia, and fibrosis of the lamina propria (Fig. 15).

Despite the broad array of endoscopic changes seen in EoE, diagnosing this disease in our country remains far from ideal. In most cases, the diagnosis is made some 7–10 years after the onset of the first symptoms, when pronounced fibrotic alterations have already developed in the esophagus,



A B

Figure 14. Pathomorphological picture of eosinophilic esophagitis, hematoxylin and eosin staining: A – intraepithelial infiltration with eosinophils, dilated intercellular spaces, magnification ×100; B – massive intraepithelial infiltration with eosinophils (more than 60 eosinophils in HPF), eosinophilic abscesses, magnification ×400

Рисунок 14. Патолого-анатомическое исследование биоптата из проксимального отдела пищевода, окраска гематоксилином и эозином: А — скопления эозинофильных лейкоцитов, расширение межклеточных пространств, увеличение ×100; В — скопления эозинофильных лейкоцитов более 60 в поле зрения, эозинофильные абсцессы, увеличение ×400

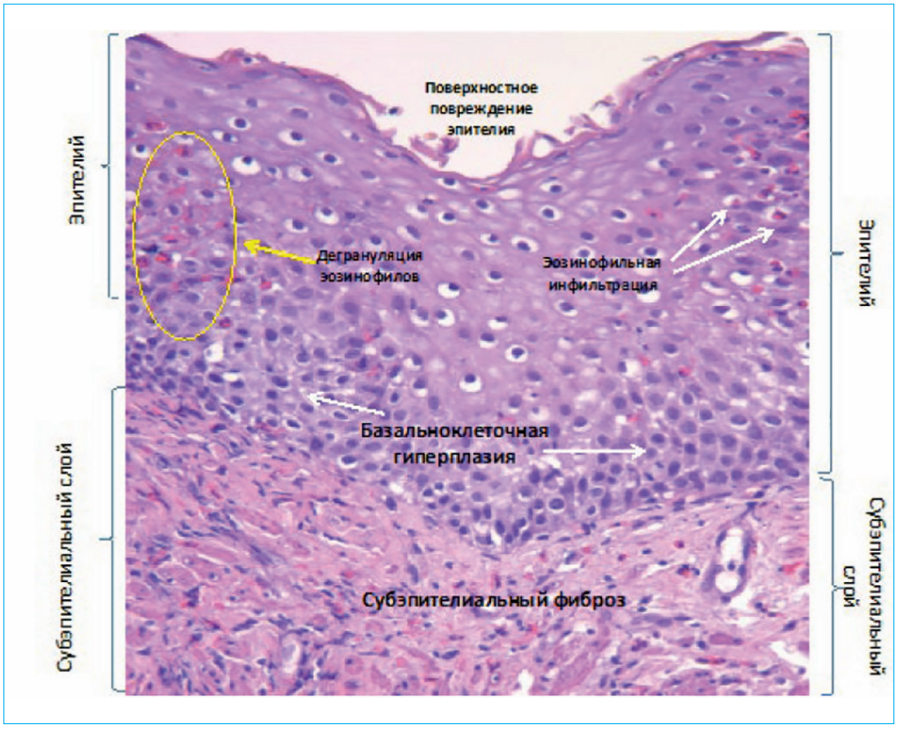


Figure 15. Histological features of eosinophilic esophagitis, hematoxylin and eosin staining, magnification ×400: intraepithelial infiltration with eosinophils, degranulation of eosinophils (yellow arrow), dilated intercellular spaces, prominent surface epithelial alteration, subepithelial fibrosis

Рисунок 15. Характерные гистологические изменения при эозинофильном эзофагите, окраска гематоксилином и эозином, увеличение ×400: эозинофильная инфильтрация, дегрануляция эозинофилов (желтая стрелка), расширение межклеточных пространств, повреждение поверхностного слоя многослойного плоского эпителия, субэпителиальный фиброз

Table 3. Frequency of occurrence of various endoscopic signs in eosinophilic esophagitis
Таблица 3. Частота встречаемости различных эндоскопических признаков при эозинофильном эзофагите

Endoscopic findings *Эндоскопический признак*	**Proportion of patients who were found to have the sign** *Доля пациентов, у которых был выявлен признак*
Edema / *Отек*	40 (85 %)
Rings / *Кольца*	27 (57,4 %)
Exudates / *Экссудат*	37 (78,7 %)
Furrows / *Борозды*	39 (83 %)
Strictures impassable to a 6 mm endoscope *Стриктуры, непроходимые для эндоскопа 6 мм*	8 (17 %)
Ankylosaurus back sign / *Спина анкилозавра*	4 (8,5 %)
Caterpillar sign / *Гусеничный след*	15 (32 %)
Multiple polypoid lesions *Множественные полиповидные поражения*	5 (10,6 %)
Erosive esophagitis stage B* *Эрозивный эзофагит стадии B**	9 (19,1 %)
Barrett's esophagus / *Пищевод Баррета*	2 (4,2 %)
Normal esophagus *Нормальная эндоскопическая картина*	3 (6 %)

Note: ** — according to Los Angeles classification.*
Примечание: ** — по Лос-Анджелесской классификации.*

and patients present to healthcare facilities with acute obstructive dysphagia.

According to our own findings (Table 3), obtained by analyzing endoscopic findings in the esophagus — EoE was graded using the EREFS scale and reflux esophagitis was graded using the Los Angeles classification — in 47 patients (43 men, 4 women, mean age — 42) with the diagnosis of "eosinophilic esophagitis" confirmed by pathomorphological evaluation (more than 15 eosinophils in a high-resolution microscope field at 3400 magnification), the most common endoscopic signs were edema, whitish exudate, and longitudinal furrows of the esophageal mucosa. Strictures were found in 8 of 47 patients (17 %). Multiple polypoid lesions were detected in 10.6 % of patients, and "ankylosaurus back" type changes — in 8.5 %. Endoscopic signs of GERD (erosive esophagitis grade B; notably, in 2 patients this coexisted with Barrett's esophagus) were diagnosed in 19 % of patients. A normal esophagus was recorded in 3 patients (6 %); in these cases, the diagnosis was established based on the overall clinical picture and biopsy findings.

Conclusion

The endoscopic features of EoE include edema, rings, furrows, exudates, strictures, multiple polypoid lesions, as well as the "caterpillar sign", "ankylosaurus back sign", mucosal fragility, and tissue resistance during biopsy. Notably, EoE-related changes can be found not only in the distal esophagus but also in the mid and proximal segments. Moreover, in some patients, particularly at early disease stages, esophageal mucosa may appear virtually normal. Modern endoscopic equipment capabilities and familiarity with the endoscopic semiotics of this condition allow for timely suspicion of EoE and performance of multiple esophageal biopsies, without which the diagnosis cannot be confirmed.

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