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Sloughing esophagitis: a spectacular histologic and endoscopic disease without a uniform clinical correlation

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Sloughing esophagitis, also currently known as esophagitis dissecans superficialis, is a degenerative disease of the squamous epithelium characterized by superficial epithelial necrosis with parakeratosis, but without inflammation, and detachment of the superficial necrotic zone from the deep viable zone. This leads to a spectacular endoscopic appearance of sloughed mucosa in streaks and patches. The cause is unknown, and the clinical characteristics are variable, ranging from incidentally findings to esophageal symptoms. The disease seems to be self-limited, as resolution of the changes was observed in the few cases for which follow-up endoscopic examinations have been reported.

Keywords: sloughing esophagitis; esophagitis dissecans superficialis; parakeratosis

Background and histology

The term "esophagitis dissecans superficialis" (EDS) was initially described over one century ago by Rosenberg,[1] whereas the name "sloughing esophagitis" was coined by Audrey Lazenby, a gastrointestinal pathologist from the University of Alabama Medical Center. This term initially appeared in two poster presentations. The first described four patients at a meeting of the United States and Canadian Academy of Pathology in 1999, and the second, which expanded the case number to 32, was presented at Digestive Disease Week in 2005.[2,3] The patients in these presentations were mostly middle-aged men who tended to be debilitated, and approximately half were immunosuppressed. The histologic changes in esophageal biopsies were impressive.[4] At low magnification, the squamous epithelium has a two-toned appearance (Fig. 1). The superficial squamous cell layer, about four to five cells thick, is necrotic and parakeratotic, with dark red cytoplasm and pyknotic nuclei. In contrast, the lower squamous cells, including the basal and parabasal layers, have cytoplasm and nuclei that appear normal. This layer is viable. The superficial necrotic layer is commonly separated from the deep viable layer. In other words, it is sloughed, leading to the name of the condition and to the remarkable endoscopic appearances of sloughed mucosa (Fig. 2). A thin layer of purulent exudate may exist at the point of separation; however, the process does not seem to have a predictable inflammatory component. In a few cases, bacteria are adherent to the necrotic zone, generally on the undersurface of the sloughed epithelium.[4] There have been a few suggestions as to why this impressive histologic change occurs, including that it is a form of contact allergy or a primary abnormality of cell adhesion molecules, but currently there is no definitive explanation. In one controlled study of 31 patients, similar to the original descriptions by Moore and colleagues, the patients tended to be debilitated, although in later descriptions patients with sloughing esophagitis appeared to only have minor medical conditions, and, in some cases, sloughing esophagitis was found incidentally.[4]

Definition

Is sloughing esophagitis the same as the esophageal disease called EDS? In some older reports of this condition, the epithelial necrosis was full

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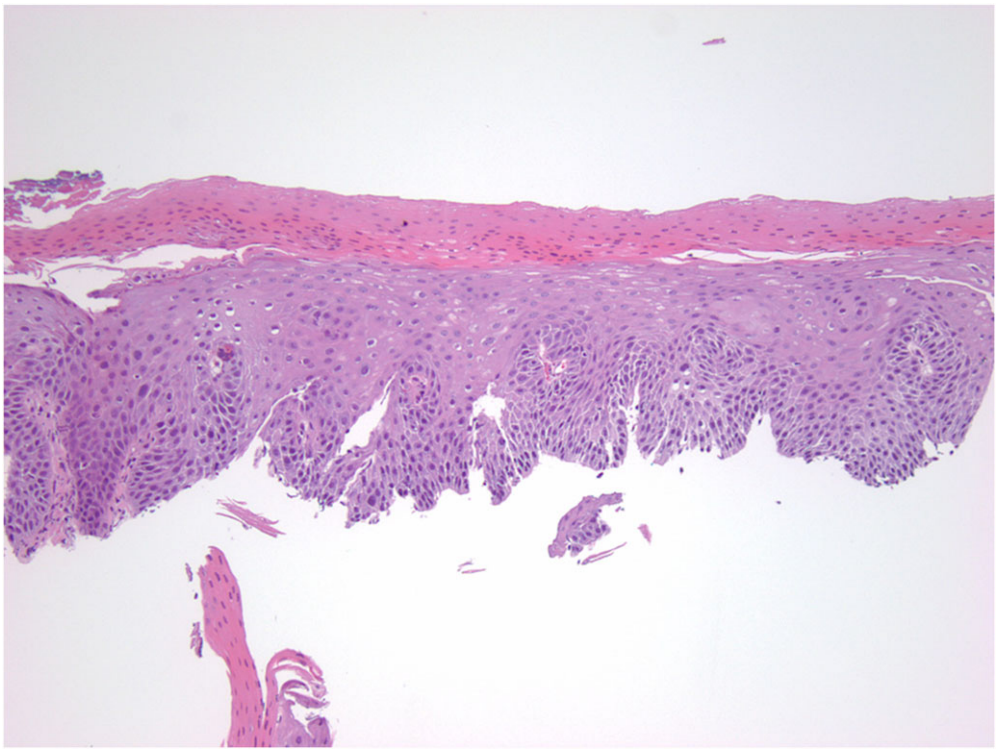

Figure 1. In the typical two-toned microscopic appearance, the necrotic superficial squamous layers have dark red cytoplasm and pyknotic or parakeratotic nuclei, while the viable lower layers have paler cytoplasm and normal open nuclei (H&E ×100). From Ref. 20.

thickness and there were chronic forms reported with stricture.[5,6] Both of these features are not typically seen in sloughing esophagitis, which seems to be an acute injury.[5,6] Furthermore, the illustrations in these papers do not conform to the changes in sloughing esophagitis detailed above. However, in two recent reports of EDS,[7,8] covering 12 and 41 patients, the histologic descriptions and photographs are identical to what was described in the patient population by Purdy *et al.*[4] In fact, the title of one of these reports used both names.[7] Therefore, for all practical purposes, as currently defined, sloughing esophagitis and EDS are the same entity.

Clinical presentation

There is no uniform clinical presentation of EDS. The presentation can vary from features incidentally found on endoscopy to esophageal symptoms, such as dysphagia or heartburn.[4,7–9] The most dramatic presentation described are reports of patients vomiting casts of mucosa.[10,11] In the largest study to date, which included 41 patients with EDS, the median age of presentation was 65 years, although 17% were younger than 40 years of age.[8] The majority of patients were Caucasian and female. The most common indication for undergoing upper endoscopy was for the evaluation of dyspepsia, dysphagia, heartburn, and regurgitation. Another case series of 12 patients (median age 65 years, 92% male, 67% Caucasian, and 34% African American) found that half of EDS patients underwent endoscopy for dysphagia or melena, but the gastrointestinal bleeding was not believed to be related.[7] Rather, EDS was found incidentally. A smaller case series from Walter Reed National Military Medical Center described five patients (80% female, median age 46 years, 40% Caucasian, 40% African American) who presented with dysphagia or reflux symptoms.[9]

Associations with sloughing esophagitis

Interestingly, an association has been reported between sloughing esophagitis and autoimmune dermatologic conditions, namely bullous pemphigoid and pemphigus vulgaris.[12] However, this is

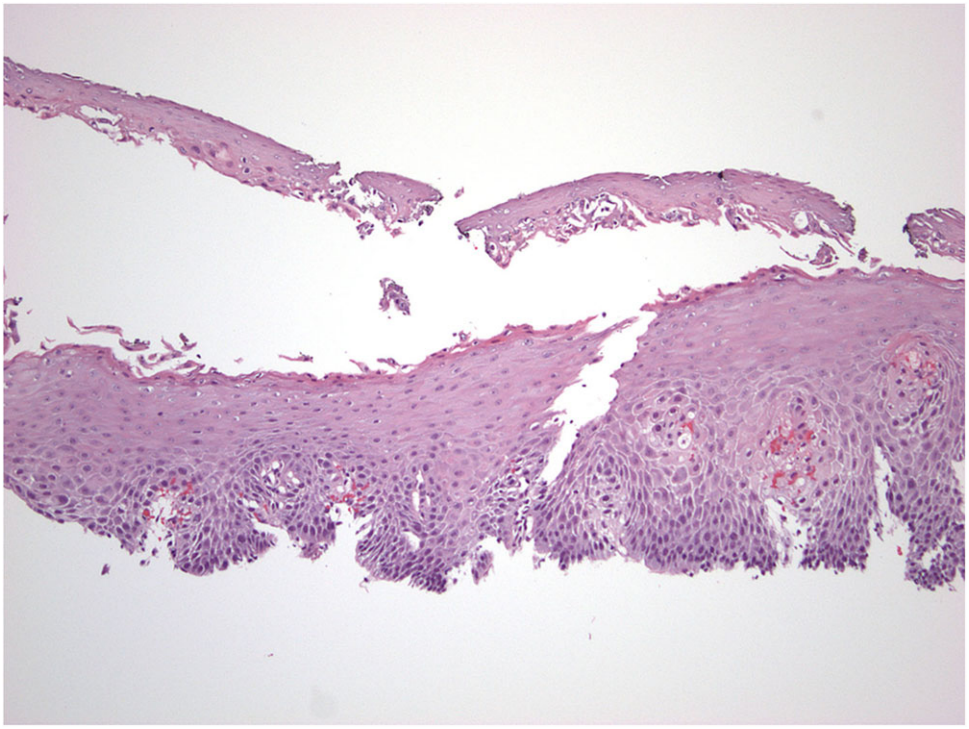

Figure 2. It is common for some biopsies to capture the separation between the necrotic superficial and viable lower layers, as in this view. This separation is what produces the spectacular endoscopic changes (H&E ×100). From Ref. 20.

a rare phenomenon, and pemphigus has been documented in only six case reports in the literature.[11–16] In the retrospective study of 41 EDS patients and the case series of 12 patients, no cases of pemphigus were reported.[7,8] In the case series of five patients, only one patient had a history of bullous pemphigoid.[9]

Concern has been raised regarding the fragility of the skin and mucosa in patients with pemphigus.[17] A Nikolsy sign may be present, which reflects stripping of the mucosa with only passage of the endoscope or use of biopsy forceps. However, there are no reported cases in the literature of esophageal perforation or hemorrhage in patients with pemphigus and sloughing esophagitis. With bullous pemphigoid, esophageal contact has led to the development of bullae in the mucosa.[17–19]

An association between some medications and EDS also exists, particularly medications that can induce topical injury, such as bisphosphonates, nonsteroidal anti-inflammatory drugs, iron, and potassium. In the study of 41 patients with sloughing esophagitis, 73% had used psychoactive medications, with selective serotonin reuptake inhibitors and selective norepinephrine reuptake inhibitors being the most commonly used.[8] It remains unclear why such medications would lead to sloughing esophagitis, and there are no current recommendations to discontinue such agents in patients found to have sloughing esophagitis.

Endoscopic appearance

The endoscopic features of sloughing esophagitis are dramatic and impressive, especially when encountered for the first time (Fig. 3). There are several findings on endoscopy reported in the literature. The appearance may be sheets of partially sloughed mucosa or crumpled, detached mucosa. It is more common to observe these findings in the distal esophagus, and they may extend proximally to either the middle or proximal esophagus.[4] Linear strips of desquamated mucosal layers may also be seen. At times, the collection of mucosa may give an appearance of an exudate and resemble esophageal candidiasis.[8,17] The circular pattern of crumpled mucosa may occasionally partially resemble eosinophilic esophagitis, but biopsies would not

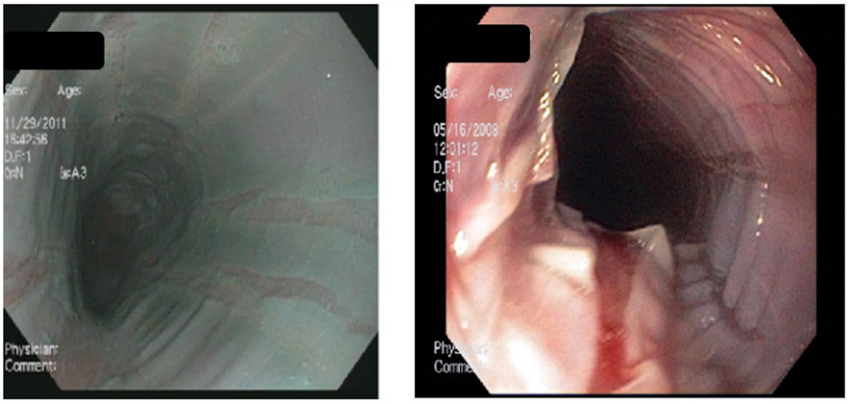

Figure 3. **Endoscopic features of two cases in which there are linear breaks with mucosal sloughing, classic features of sloughing esophagitis. From Ref. 9.**

reveal dense eosinophilic infiltrates. The detached mucosa can easily be peeled with biopsy forceps, although this is unnecessary. In a recent review article, Hart *et al.*[8] proposed three endoscopic criteria for sloughing esophagitis: strips of sloughed mucosa measuring greater than 2 cm, normal underlying mucosa, and lack of ulceration in adjacent tissue.

Management

As the underlying pathogenesis of sloughing esophagitis is unknown, there is no clear consensus for management of this condition. If it is associated with an autoimmune dermatologic condition, treatment of the underlying disorder may improve esophageal findings. In patients prescribed medications known to induce topical esophageal injury, cessation of these medications or switching to other agents can be considered, when possible. Given the desquamated appearance of the mucosa, acid suppressants are often prescribed as treatment. Although such agents may not resolve the esophagitis, at the very least, a reduction in acid exposure may assist in healing the mucosa. It is noteworthy, however, that, in several of the case series of sloughing esophagitis, a proportion of patients were on proton pump inhibitors (PPIs) at the time of diagnosis, raising the possibility that PPIs may not have a role in the treatment of sloughing esophagitis.[8,9]

Among patients with sloughing esophagitis in which follow-up occurred, healing has been documented in as short as 8 weeks, suggesting that it is a benign condition. In the case series of five patients, all improved clinically, and, in the only patient who had endoscopic follow-up, resolution of the findings was noted. In the case series with 12 patients, 80% (4/5) had resolution on follow-up endoscopy.[7] In the retrospective study of 41 patients, 34% had follow-up, with resolution noted in 86% of patients after a median of 4 months.

Conclusions

Sloughing esophagitis, or EDS, is an uncommon condition characterized endoscopically by features of sloughed-off mucosa and histologically by parakeratosis and necrosis. There is no known treatment for sloughing esophagitis; however, its natural course appears benign, as the majority of patients experience resolution within a relative short period.

Conflicts of interest

The authors declare no conflicts of interest.

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