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Case report

Esophageal Leukoplakia and Its Clinical Significance: Does It Imply Risk?

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Abstract

Esophageal leukoplakia is an extremely rare condition. It typically occurs in patients who smoke, frequently consume alcohol, or have chronic mucosal irritation from gastroesophageal reflux. Endoscopically, well-circumscribed whitish plaques are commonly observed in the middle or distal third of the esophagus. These lesions can be easily mistaken for glycogenic acanthosis, esophageal papilloma, eosinophilic esophagitis, or Candida esophagitis. Timely recognition and management are essential, as esophageal leukoplakia is considered a precursor to squamous cell carcinoma.

Keywords

Leukoplakia, esophagus, esophageal diseases, epidermolytic hyperkeratosis, endoscopy, squamous cell carcinoma.

INTRODUCTION

Leukoplakia is the term used to describe whitish plaques or patches on mucous membranes that cannot be "scraped off" and are not clinically characterized as another disease. Its oral form is the most frequently described in the literature, with a worldwide prevalence of 4.11%; it is characteristically painless, associated with alcohol consumption or smoking, and is a known risk factor for squamous cell carcinoma[1].

It is a rare finding in the esophagus, described mainly in case reports and small series, with an established prevalence of 0.19% in patients undergoing biopsy for any other reason[2-4]. Its risk factors are similar to those of the oral form, primarily smoking, alcohol consumption, and chronic mucosal irritation. Endoscopically, it is characterized by well-demarcated whitish lesions with surrounding healthy tissue, located mainly in the middle or distal third of the esophagus, with local or diffuse distribution. The histological term defining this entity is *epidermoid metaplasia*, characterized by squamous epithelium with orthokeratosis and a prominent granular cell layer, which is why it can also be found in the literature as *esophageal hyperkeratosis*[5]. Its differential diagnoses include glycogenic acanthosis, esophageal papilloma, eosinophilic esophagitis, and candida esophagitis, which can be differentiated using Lugol's staining, as the latter stain positive, whereas epidermoid metaplasia is resistant to it[4].

Although leukoplakia can be an incidental finding in asymptomatic patients, Kamboj et al.[6] showed that two-

thirds of patients had dysphagia at the time of diagnosis and that in up to 25% of patients, it could occur before, concomitantly with, or after the diagnosis of esophageal squamous cell carcinoma—a considerably high risk compared to other entities associated with squamous cell carcinoma, such as esophageal lichen planus and achalasia, with risks of 6.1% and 2.7%, respectively[7,8]. It is a precursor of squamous cell carcinoma, and sometimes high-grade dysplastic areas can be observed within it, making it unreliable to base decisions solely on biopsies, as samples might be taken from unaffected areas within the lesion. Targeted sequencing techniques support this. The detection of mutations, including that of the tumor protein P53 (TP53) in epidermoid metaplasia samples, corroborates the clonal relationship between these entities[9]. Additionally, Sang et al. showed that leukoplakia is an independent risk factor for non-curative resection in patients with high-grade intraepithelial neoplasia, making detection and early resection, when indicated, even more important[10].

CASE REPORT

A 72-year-old male, a heavy smoker, presented with a 6-year clinical history of regurgitation and heartburn. His medical history recorded no other positive findings. Physical examination was normal, including a thorough evaluation of the oral cavity and neck. An esophagogastroduodenoscopy (EGD) revealed a flat lesion (Paris 0-IIb) measuring 30 mm, suggestive of leukoplakia in the distal third of the esophagus (immediately above the gastroesophageal junction) (**Figure 1**). The lesion borders were biopsied, and the histopathological report indicated esophageal mucosa with a focal area of leukoplakia with epithelial hyperplasia, parakeratosis, and inflammation. Stains with methenamine silver and periodic acid-Schiff (PAS) were negative, and no changes suggestive of dysplasia or carcinoma were reported (**Figure 2**). Given the lesion size and the potential risk of malignant transformation, the patient underwent endoscopic submucosal dissection using a tunneled technique (ESTD), achieving negative resection margins. Prophylactically, due to the circumferential resection, a short course of steroids was indicated, and a covered self-expandable metal stent was placed, which was removed at the fourth week.

DISCUSSION

Few cases of this entity have been reported in the literature, so there are no guidelines or consensuses to individualize management. Ezoe et al. reported a high rate of synchro-

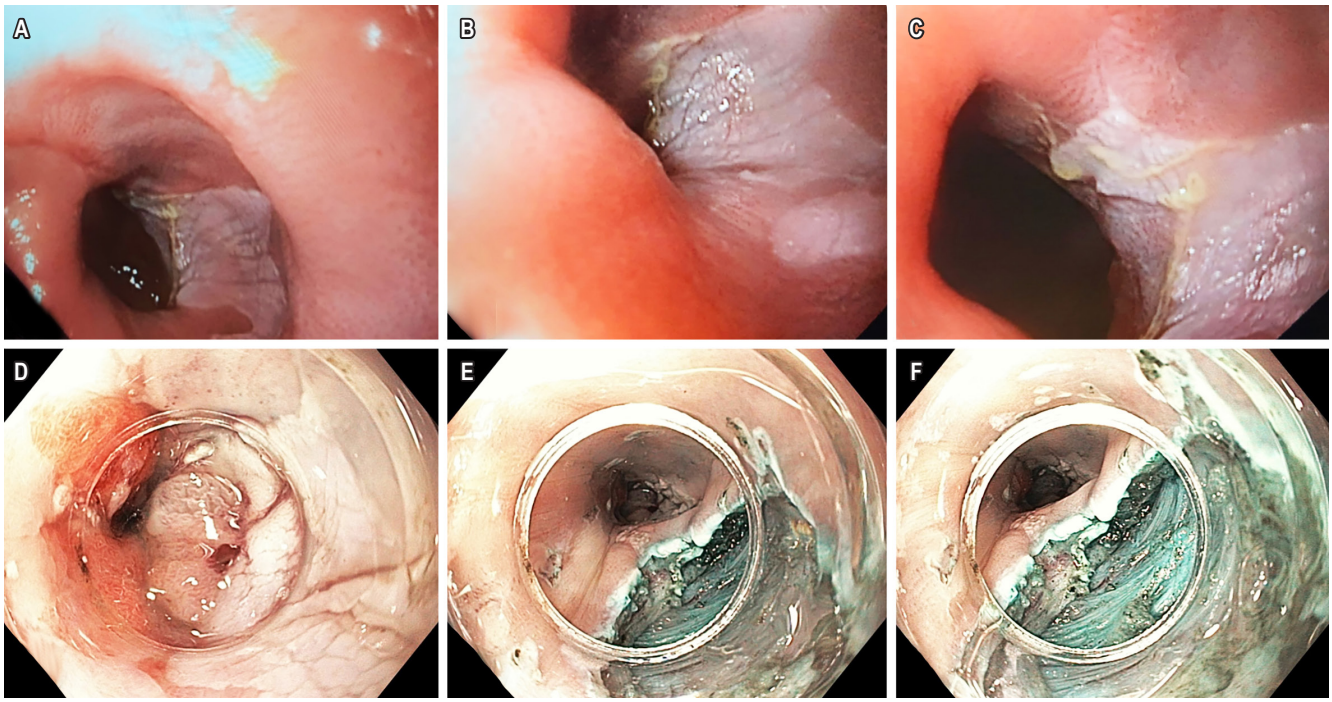

Figure 1. Clinical case examinations. **A, B, and C.** EGD showing a 30 mm lesion in the distal esophagus characterized as a well-defined whitish plaque with surrounding normal mucosa, suggestive of leukoplakia. **D.** Elevated leukoplakia with hyaluronic acid, saline, and methylene blue before dissection viewed through Cap. **E and F.** Endoscopic submucosal dissection of esophageal leukoplakia. Resection bed. Images property of the authors.

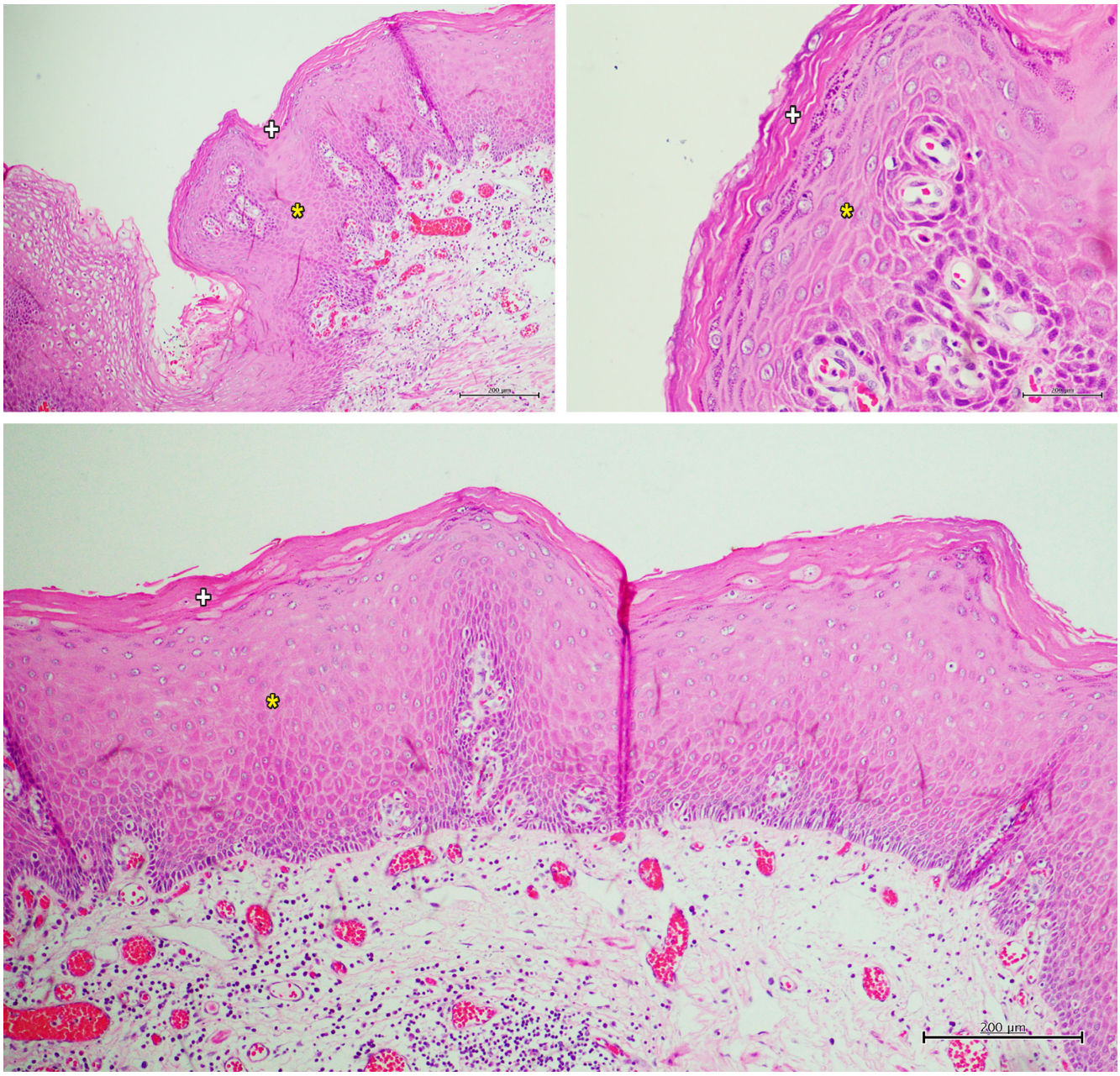

Figure 2. Histological findings. Esophageal mucosa with a focal area of leukoplakia with epithelial hyperplasia (*), parakeratosis (+), and inflammation. No changes suggestive of dysplasia or carcinoma were reported. Hematoxylin and eosin stain. Images property of the authors.

nous or metachronous esophageal and oropharyngeal squamous cell carcinoma in a case series[11]. High-grade squamous dysplasia or squamous cell carcinoma was found in 17% of the patients. Meanwhile, Aida et al. found that epithelial cells within lesions with orthokeratotic dysplasia have greater telomere attrition and a higher number of anaphase bridges, which translates to greater instability and a tendency toward changes with malignant potential[12]. This highlights the importance of recognizing and managing these lesions early.

Most authors recommend strict endoscopic surveillance every 1 to 6 months for cases without demonstrated dysplasia, or ablation with radiofrequency or argon plasma coagulation; however, in the presented case, although we found no foci of dysplasia or carcinoma in situ in the biopsies taken from the lesion, the size and the fact that the entire

lesion had not been explored histologically (possibility of high-grade dysplastic foci not represented in the biopsy) led us to consider endoscopic submucosal dissection as the appropriate management, which also ensures a higher rate of R0 resection compared to other techniques. In the absence of recommendations with sufficient evidence quality, the choice of management strategy is left to the clinician's discretion, based on what is most suitable and adjusted to the availability of local resources.

CONCLUSION

When facing a patient with esophageal leukoplakia, it is essential to conduct a thorough differential diagnosis, as it carries a clear association with high-grade dysplasia and cancer. Management is variable, ranging from strict endoscopic surveillance to endoscopic submucosal dissection, with the goal of achieving en bloc resections with free margins and a higher R0 rate. Until formal consensus recommendations are available, each case must be individualized, and management defined according to the availability of local resources.

Ethical Considerations

This study does not expose information that would allow patient identification; therefore, it does not require informed consent or approval protocol by an institutional ethics committee, in accordance with the Declaration of Helsinki and Resolution 008430 of October 4, 1993.

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Conflicts of Interest

The authors declare no conflicts of interest.

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