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Brief report

BRIEF REPORT

White esophageal lesions in a patient with scleroderma: epidermoid metaplasia

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Case presentation

We report the case of a 67-year-old female with a 24-year smoking history who initially underwent esophagogastroduodenoscopy (EGD) in 2012 for gastroesophageal reflux disease (GERD), which demonstrated short-segment Barrett's esophagus without dysplasia. Repeat EGD 6 years later showed severe reflux esophagitis (LA grade D). She was subsequently diagnosed with limited systemic sclerosis (CREST syndrome) on the basis of Raynaud's disease, sclerodactyly, telangiectasias, seropositivity (anti-CENP-A, anti-CENP-B), and pulmonary hypertension. High-resolution esophageal manometry showed esophageal body aperistalsis with a hypotensive lower esophageal sphincter (LES) (Figure 1).

Follow-up EGD after 1 year of acid suppression with a high-dose proton pump inhibitor revealed a dilated esophagus with translucent, well-demarcated white scaly lesions throughout the esophagus (Figure 2). Esophageal biopsies showed areas of basal cell hyperplasia with acanthosis, hypergranulosis, hyperorthokeratosis, and focal parakeratosis, consistent with epidermoid metaplasia (Figure 3). She was started on a prokinetic agent (prucalopride, 5HT3 agonist) for symptoms of reflux and dysphagia. Repeat EGD 3 months later showed a slight improvement in esophageal mucosal appearance with mucosal biopsies showing acute chronic inflammation with parakeratosis, but no dysplasia, and no epidermoid metaplasia.

Discussion

Esophageal leukoplakia is characterized by Lugol-voiding white patches or plaques that cannot be scraped off in the esophagus, analogous to oral leukoplakia in the oropharynx [1]. Epidermoid metaplasia is considered the histopathologic correlate and is defined by compact hyperorthokeratosis and a well-defined granular layer. This finding is rare, with an estimated prevalence of <1% based on the examination of 1,048 consecutive biopsy samples in a tertiary center [2]. Proposed risk factors include chronic reflux, heavy alcohol use, tobacco smoking, and achalasia [1, 3–5]. There is an association with esophageal squamous neoplasia, with case series reporting 17%–100% of patients having synchronous or metachronous squamous esophageal neoplasia at time of biopsy [3, 4]. More recently, targeted next-generation sequencing has demonstrated shared genetic alterations between epidermoid metaplasia and esophageal squamous neoplasia, suggesting that epidermoid metaplasia is a potential precursor lesion and progression may be predicted by the presence of a *TP53* mutation [6]. There is a paucity of long-term outcome data on this condition and the magnitude of the risk of progression is still not known. Singhi *et al.* report on a median 22 (range 4–99)-month follow-up on 12 patients without dysplasia or squamous cell carcinoma at the time of diagnosis and 9 (75%) patients had evidence of persisting disease on repeat biopsy, with none progressing to dyspasia or carcinoma.

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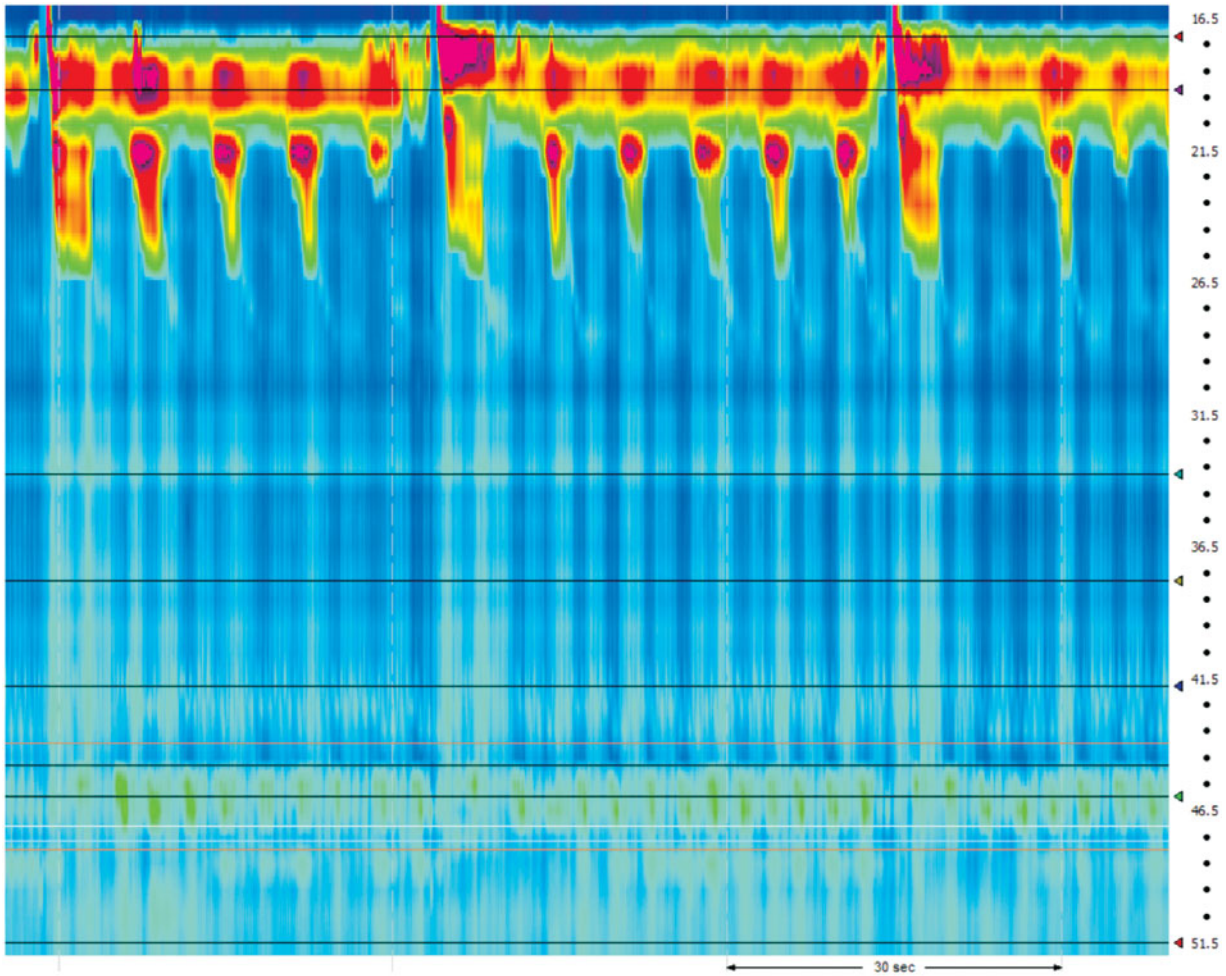

Figure 1. Classic 'scleroderma esophagus' with aperistalsis through the esophageal body and hypotensive lower esophageal sphincter

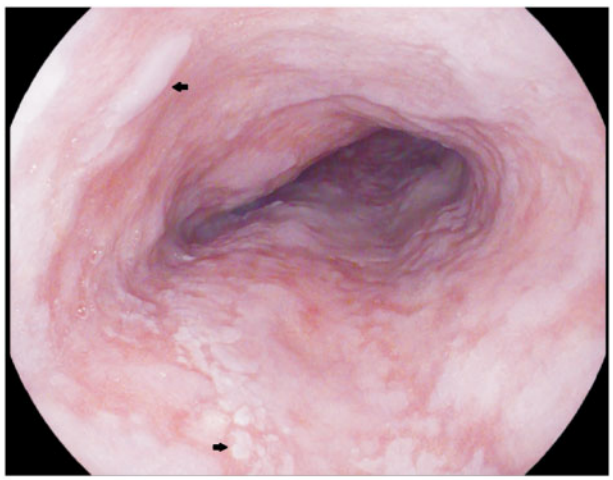

Figure 2. Dilated esophagus with translucent, well-demarcated white scaly lesions throughout (black arrows)

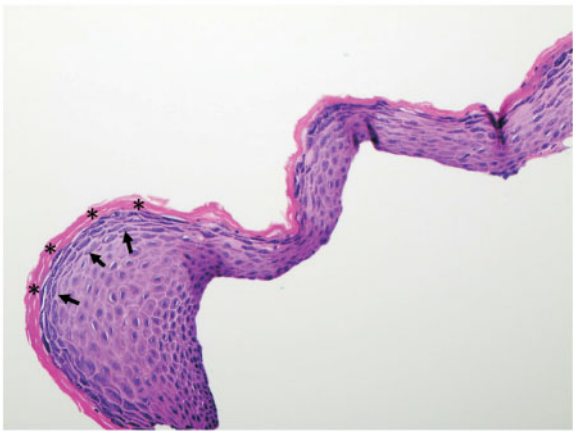

Figure 3. Midesophageal mucosal biopsy demonstrating areas of compact hyperorthokeratosis (*) and a well-defined granular layer (arrows)

Esophageal leukoplakia has previously been reported in scleroderma patients [7]. While our patient was a long-standing smoker, reflux could also be implicated, as suggested by Fukai *et al.* [1]. Our patient had evidence of 'scleroderma esophagus' with aperistalsis through the esophageal body and hypotensive LES pressure, which would predispose to acid reflux, as well as stasis-related damage from the inability to clear refluxate in the setting of ineffective secondary peristalsis [8]. She was started on a prokinetic agent and had no evidence of epidermoid metaplasia on repeat biopsy after 3 months. This intervention supports acid reflux as a causative agent in the genesis of epidermoid

metaplasia and supports the use of aggressive acid suppression or prokinetic agents in the management of this condition.

Despite the apparent resolution of her epidermoid metaplasia, we plan on enrolling her for indefinite dysplasia surveillance, given the uncertainty regarding long-term outcomes, as well as the presence of unmodifiable risk factors (e.g. dysmotility-related esophageal stasis and esophageal acidification, and smoking history).

Conflicts of interest

None declared.

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