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The Coexistence of Primary Laryngeal Pemphigus, Oesophageal Inlet Patch and Oesophageal Stricture Presenting with Odynophagia

Case Report

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Abstract

An 80 year old male patient presented with severe odynophagia and retrosternal discomfort that resulted in a 5 kg weight loss in two months. The patient had a history of total gastrectomy-esophagojejunostomy and radiotherapy for gastric carcinoma, 22 years previously. Endoscopy revealed lesions located on the epiglottis and arytenoids. Histopathology of lesions was pemphigus vulgaris while the presence of gastric mucosa in samples was suggestive of Inlet Patch. We present a coexistence of primary laryngeal pemphigus and Inlet Patch.

Key Words: Pemphigus, laryngeal pemphigus, inlet patch

Introduction

Pemphigus is an autoimmune disease which involves both skin and mucosal membranes. The pemphigus lesions are commonly located in the oral cavity and primary laryngeal manifestation is extremely rare (1, 2). Although the etiology in most cases is ambiguous, many factors; including drugs, physical agents (burns), infections (herpes virus), contact dermatitis, neoplasms, emotional stress, and ultraviolet radiation have been reported to trigger the disease (3-5).

The inlet patch is an area of hetero topic gastric mucosa located in the esophagus. It is most commonly located in the postcricoid portion of the esophagus or just below the level of the upper esophageal sphincter (6, 7). Although inlet patch generally remains asymptomatic, in some cases complications related to acid secretion such as esophagitis, ulcer, web, and stricture can occur (6, 8-10).

Herein, we present the coexistence of primary laryngeal pemphigus and esophageal inlet patch in a patient who had total gastrectomy 22 years previously. Being the only acid secretory source in this particular patient, inlet patch may play a role in the pathogenesis of laryngeal pemphigus apart from other previously described factors.

Case Report

An 80 year old male patient presented with severe odynophagia which resulted in a 5 kg weight loss in two months. He also complained of sore throat, hoarseness, troublesome cough and retrosternal discomfort. The patient had a history of total gastrectomy-esophagojejunostomy operation and adjuvant radiotherapy due to the diagnosis of gastric carcinoma, 22 years previously. No chronic diseases or medication was reported. The oral and nasal mucosa was healthy except for slight hyperemia on the left buccal mucosa. Fiberoptic laryngoscopy revealed supraglottic lesions which were remarkable due to pale and grayish colored membranes mainly located on the epiglottis and arytenoids. The patient underwent direct laryngoscopy and esophagoscopy under general anesthesia for determining the extent of the lesions and tissue biopsy. The mucosal lesions

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were very fragile and easily detached from the underlining surface even with gentle instrumentation (Figure 1). During the esophagoscopy, a stricture formation involving the postcricoid region and upper esophageal sphincter was observed and was treated successfully with bougie dilatation (Figure 2). Under the stricture, a flat salmon-colored patch was identified and it was also biopsied (Figure 3). Histopathologic examinations of the biopsies obtained from the supraglottis revealed pemphigus vulgaris (Figure 4) while the presence of gastric mucosa in the later samples were suggestive of inlet patch (Figure 5). Co-existence of inlet patch and stricture raised concern about acid exposure were suspected, thus we performed a 24-hour pH monitoring with wireless Dx -pH system (Respiratory Technology Corporation (Restech), San Diego, California). The patient had 22 events when the pH was under 5.5. The longest episode was 5.39 minutes and %pH below baseline in upright and supine positions were 1.22% and 0.78% respectively. He pushed the cough symptom button 42 times and heartburn button 4 times and all heartburn symptoms were related with pH events.

Knowing that the patient had total gastrectomy 22 years previously, theoretically these acid exposures could only be related to the inlet patch which was histopathologically diagnosed. Therefore, lansoprazole 30 mg twice a day was added to the patient's medical therapy which consisted of prednisolone 60 mg/day for 10 days. The prednisolone was tapered off after the tenth day and the lansoprazole was continued for 3 months. The patient'symptoms improved at the 2nd month follow up.

Discussion

Pemphigus is a rare autoimmune, muco-cutaneous bullous disease. The mean age of presentation is 40-50 years of age and it has an increased incidence in Mediterranean people (3, 11). Pemphigus vulgaris is the most common form of pemphigus that begins with mucosal involvement in more than half of the patients. Oral mucosa is the most frequently involved region; however, the oropharynx, larynx, nasal mucosa, and esophagus may also be involved (12, 13). Robati et al. (14) reported 26.8% ear, 36.7% nose, 90.2% mouth, 61% pharynx and 58.5% larynx involvement in pemphigus vulgaris patients. Hale and Bystryn (15) described 40% laryngeal involvement. Although, laryngeal manifestations can be seen during the course of the disease, pemphigus with primary laryngeal manifestations is extremely rare (1, 2). Hoarseness is the first symptom of the laryngeal involvement in many cases (12, 16). The symptoms of the presented case were odynophagia, sore throat, hoarseness, troublesome cough, and retrosternal discomfort for 2 months. The pemphigus vulgaris lesions were limited to the larynx and

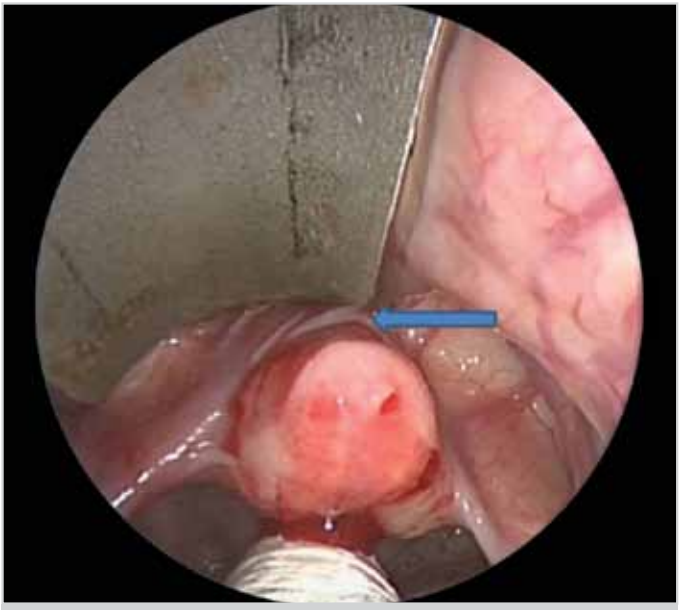

Figure 1. Pemphigus lesions which are remarkable with pale and grayish colored membranes and mainly located on epiglottis and arytenoids

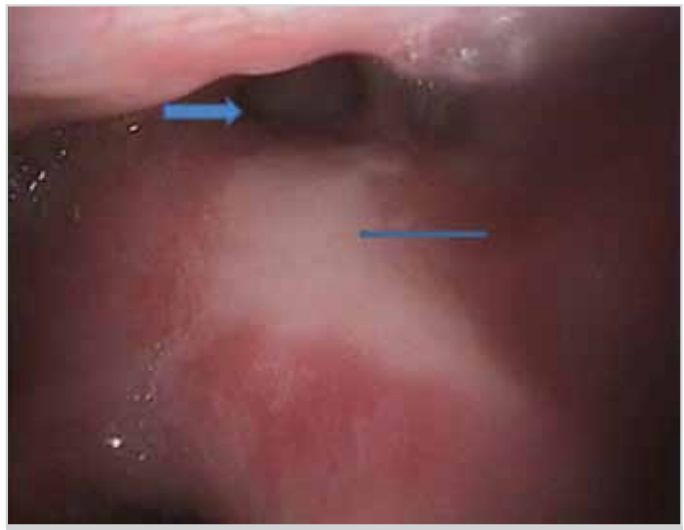

Figure 2. Stricture formation involving the postcricoid region and upper esophageal sphincter (thick arrow) and pemphigus lesion on arytenoid (thin arrow)

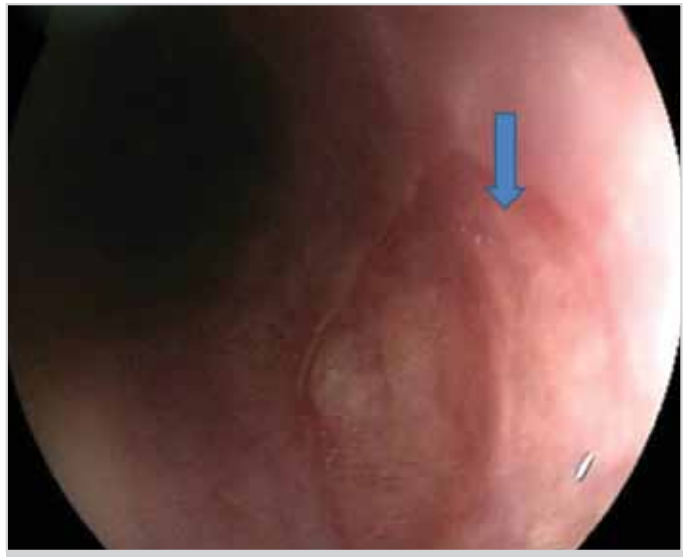

Figure 3. Salmon colored inlet patch

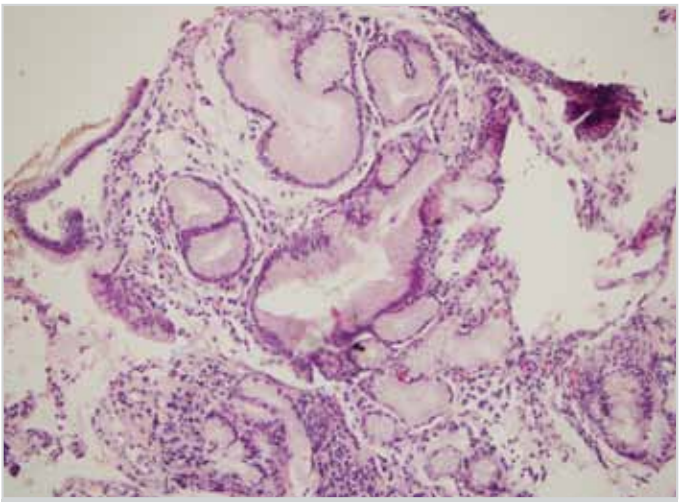

Figure 4. Biopsy specimen of laryngeal mucosa showing supra-basal separation in upper part, fibrin discharge and infiltration of inflammatory cells in lower part (x20)

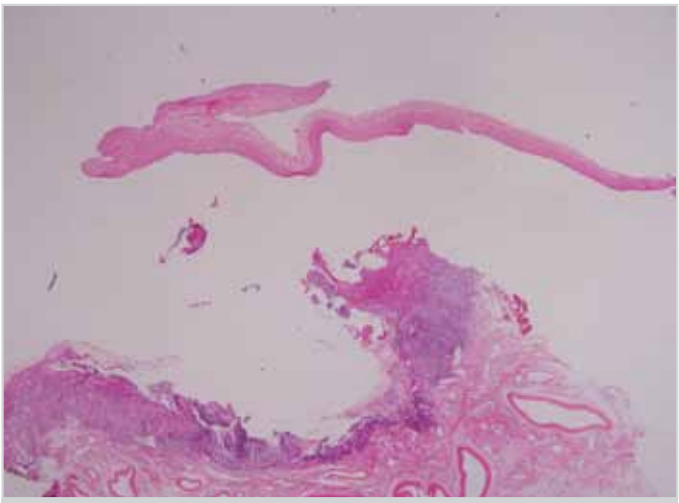

Figure 5. Biopsy from inlet patch in proximal esophagus, showing primarily gastric-type columnar mucosa with slight lymphoid infiltration (x100)

arytenoids, no other mucosal or cutaneous lesions were present at the time of diagnosis.

Heterotopic gastric mucosal patches are congenital gastrointestinal anomalies and have been reported to occur anywhere along the gastrointestinal system as well as in locations outside the gastrointestinal system (17). The heterotopic gastric mucosa located in the esophagus is specifically named as inlet patch . The inlet patch is most commonly located in the postcricoid portion of the esophagus or just below the level of upper esophageal sphincter (6, 7). The reported incidence of inlet patch in the endoscopic examination, ranged from 0.29 to 10%, while a higher incidence of up to 70% has been reported in autopsy studies (17). Moreover, Maconi et al. (18) revealed that the reported prevalence of inlet patch may even change according to the examiners' awareness. They reported that operators who are aware of this entity diagnose inlet patch more frequently than operators who are not, 2.27% and 0.29% respectively. The origin of heterotopic gastric mucosa is thought to be congenital in nature and inlet patch is thought to represent esophageal columnar embryologic remnants that had failed to transform to squamous lining during the fetal development period. Gastric mucosa containing cardiac, antral and potentially acid-secreting fundic mucosa can be found by microscopic evaluation (17). Inlet patch can also cause dysphagia, globus sensation, hoarseness, sore throat, throat cleaning, chronic cough and vocal fold dysfunction (17, 19). In the presented case, upper esophageal inlet patch lesion was encountered during direct laryngo-osephagoscopy. The patient had the symptoms of sore throat, hoarseness, troublesome cough, retrosternal discomfort and dysphagia concordant with the literature, while the odynophagia was thought to be more relevant to the stricture formation.

The pemphigus etiology is unclear in most cases but it can be induced by many factors including drugs, physical agents (burns), infections (herpes virus), contact dermatitis, neoplasm, emotional stress, and ultraviolet radiation (3, 5). Frangogiannis et al. (20) reported a case of primary laryngeal pemphigus induced by enalaprile. The presented patient was not taking one of the drugs which have been reported to induce the pemphigus, hence we focused on the other possible factors, such as radiation. Mul et al. (21) mentioned that pemphigus might be considered as a radiotherapy-induced side effect. Bar-Sela et al. (3) reported a case of mucosal and esophageal pemphigus vulgaris without skin manifestations that is induced by radiotherapy. However it has been 22 years since the radiotherapy which the patient had for gastric cancer. Moreover, the larynx was not included in the target zone.

Pemphigus can be triggered by other physical agents. In spite of the lack of published data, we hypothesized that acid may be one of these agents. The co-existence of inlet patch, stricture and the anatomic closeness of the pemphigus lesions were also supportive findings for our hypothesis. Therefore, we performed a 24-hour pH monitoring with wireless Dx-pH system© which has a minimally invasive catheter featuring an ion flow sensor that is able to measure accurately the pH in both liquid and aerosolized droplets (22). Since we were attempting to reveal the acid exposition, we accepted the threshold pH level of 5.5, instead of 4.5 when the pepsin is thought to be active. As a result, we showed a hyper acidic situation in the upper airway by 24-hour pH monitoring and, since the patient doesn't have a stomach, we concluded that the inlet patch was the source of this acid secretion. Depending on the pH monitoring results we added a proton pump inhibitor (lansoprazole 30 mg twice a day) to the patient's medical therapy which mainly consisted of oral corticosteroids. The symptoms and physical findings of the patient were relieved at the 2nd month follow up.

Conclusion

Several factors have been reported to induce laryngeal pemphigus. Acid exposure, even originating from inlet patch as in this presented patient, may play a role as a physical agent. Being the first case report in the English literature regarding this issue, this report may hopefully lead to new researches on the relationship between pemphigus and acid exposure.

Conflict of Interest

No conflict of interest was declared by the authors.

Peer-review: Externally peer-reviewed.

Informed Consent: Written informed consent was obtained from patients who participated in this case.

Author Contributions

Concept - Ö.K.; Design - Ö.K., B.A.; Supervision - S.K., M.G.; Funding - Ö.K.; Materials - Ö.K., B.A.; Data Collection and/or Processing - Ö.K.; Analysis and/or Interpretation - Ö.K., S.K., B.A., A.U., Ö.G., M.G.; Literature Review - Ö.K.; Writing - Ö.K.; Critical Review - M.G.

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