Successful Treatment of Extensive Esophageal Squamous Papillomatosis With Cryotherapy

Mohammad Alomari, MD, Vaibhav Wadhwa, MD, Pablo Bejarano, MD, Patrick Amar, MD, and Tolga Erim, DO

ABSTRACT

Esophageal squamous papilloma is a rare endoscopic finding, and esophageal squamous papillomatosis (ESP) is considered exceptionally rare, with only a limited number of cases reported to date. There is a paucity of literature about the management of these lesions, and it remains largely controversial. We report a 61-year-old man who presented for endoscopic treatment of ESP detected during endoscopic evaluation for heartburn. Given the potential risk of malignant transformation, a decision was made to proceed with spray cryoablation, requiring a total of 3 sessions of ablative therapy. The histopathological assessment confirmed the diagnosis, and the specimens tested negative for all low- and high-risk human papillomavirus subtypes. Follow-up endoscopies revealed near-complete resolution. To our knowledge, the present report describes the second successful treatment of ESP using endoscopic spray cryotherapy.

INTRODUCTION

Esophageal squamous papilloma is a very rare endoscopic finding characterized histologically by finger-like projections of the hyperplastic squamous epithelium covering a connective tissue core. Although most lesions are solitary, esophageal squamous papillomatosis (ESP) has also been described in the literature. The etiology remains largely unknown; however, it is suggested that ESP may result from chronic mucosal irritation and possibly human papillomavirus (HPV) infection. Optimal management of these lesions has not been well established. Useful treatment options reported have been endoscopic mucosal resection, laser removal, and radiofrequency ablation. Our case presents the eradication of ESP using endoscopic spray cryotherapy (SCY), and underscores the importance of early detection and treatment of ESP to prevent progression to esophageal carcinoma, suggesting SCY as an effective and reasonable option.

CASE REPORT

A 61-year-old man was referred to our institution for endoscopic treatment of ESP discovered incidentally during the workup of heartburn symptoms. His medical history was significant for essential hypertension, type II diabetes mellitus, and coronary artery disease, for which he had been treated. The patient admitted to social drinking but never smoked. His physical examination showed no abnormality. Laboratory evaluation was unremarkable.

After discussion with the family and patient regarding different treatment options, a decision was made to proceed with cryospray ablation using liquid nitrogen. Esophagogastroduodenoscopy performed at our center demonstrated evidence of Los Angeles grade B esophagitis at the gastroesophageal junction along with extensive ESP extending from 34 to 38.5 cm from the incisors, in a hemicircumferential pattern, with numerous (>50) sessile, verrucous lesions up to 1.5 cm in size (Figure 1).
Endoscopic visualization identified the ablation site. Ventilation tubing was inserted over a guidewire, followed by reinsertion of the endoscope. Subsequently, the ablation catheter was inserted via the working channel, and a total of 2 sites were ablated. SCY using the truFreeze System (CSA Medical, Lexington, MA) was used with liquid nitrogen cryogen applied for 20 seconds after the first appearance of a frosting effect. During the procedure, continued suction ventilation of gases was performed, and the tissue was allowed to thaw before reablating. Ablation was repeated in a likewise fashion at each site for a total of 2 cycles. After performing SCY, the ventilation tubing was removed, and a reddish changes indicative of ablated mucosa were observed. The patient tolerated the procedure well with no complications.

Pathologic examination of all biopsy sets revealed mostly transversally cut papillae with congested fibrovascular cores of a squamous papilloma that support the diagnosis of ESP without evidence of dysplasia or malignancy (Figure 2). Chromogenic in situ hybridization for HPV was performed, and cells were negative for low- and high-risk HPV subtypes.

He underwent 3 sessions, 2–4 months apart, of liquid nitrogen cryospray ablation with standard freeze-and-thaw cycles. Follow-up endoscopy 3 months after the last treatment session revealed near-complete resolution (Figure 3). A solitary 2-mm squamous papilloma discovered using narrow-band imaging was removed by cold forceps (Figure 4). Subsequent surveillance upper endoscopies showed no further evidence of squamous papillomas. However, there was a healthy-appearing scar tissue at the site of previous cryotherapy. Biopsies from this scar tissue disclosed a benign esophageal squamous epithelium with no significant pathological changes.

DISCUSSION

Squamous papilloma is a rare fleshy pink-colored epithelial tumor first described by Adler et al in 1959 as a wart-like solitary lesion located mostly in the mid to distal esophagus.24 Analysis of the previous endoscopy series showed a prevalence ranging from 0.01% to 0.45%.1 It is more common among middle-aged men with a reported higher prevalence in Europe, accounting for approximately 70% of cases.17 Near-circumferential involvement of the esophagus, as in our patient, is extremely rare.

The etiology of ESP remains unclear, although roles of chronic mucosal irritation and HPV infection have been proposed. Prolonged chemical and mechanical mucosal irritation may generate a cellular damage-repair response followed by hyperregeneration. This hypothesis seems supported by the higher prevalence of gastroesophageal reflux disease, previous esophageal dilation, prolonged nasogastric intubation, and nitrosamine exposure among patients with ESP.17,18,25,26 Infection with HPV may also be associated with an increased risk of having esophageal squamous cell papillomas based on some observational studies.20,21 Nonetheless, it remains controversial because of extreme prevalence variability among the reported cases.22 Others suggested that tobacco and alcohol abuse are associated with an increased lifetime risk of having esophageal squamous papillomas.2,17

Patients are typically asymptomatic but can rarely present with heartburn or dysphagia.3,4,9,13,15,27 Diagnosis is usually made during upper endoscopy performed for a different indication as they appear as single or multiple round lesions that rarely exceed 1 cm in diameter. Histologically, they appear as finger-like projections of squamous epithelial cells with a connective tissue core containing small blood vessels.21 Diffuse esophageal involvement with multiple lesions is exceedingly rare.
Examination of the existing literature has shown a variable clinical course, ranging from spontaneous regression to the development of squamous cell carcinoma. Although it is unknown whether solitary esophageal papillomas are premalignant lesions because of the highly variable clinical course, ESP carries a significant potential of malignant transformation, as squamous cell carcinomas were identified in almost half of the reported cases. Thus, early diagnosis and treatment remain imperative.

Considering the benign nature of solitary lesions, treatment has been reserved only for symptomatic cases. Endoscopic resection with biopsy forceps, snare polypectomy, and cautery have been used for small single lesions. Treating multiple lesions has been challenging, and the optimal management and surveillance guidelines remain unclear because of the paucity of reported cases. Some patients with extensive ESP underwent esophagectomy because of associated dysplasia and progression to carcinoma. Nevertheless, previous methods used include endoscopic resection, laser removal, radiofrequency ablation, and cryotherapy, with variable rates of failure and recurrence.

SCY delivers cold nitrogen gas via a catheter introduced into the esophagus through an accessory channel of an upper GI endoscope. Esophagoscopy is performed under monitored anesthesia care, and cold nitrogen gas is sprayed over the affected portion of the esophagus under direct visualization. Freezing of the esophageal mucosa is evidenced as white cryoburn with sharply demarcated margins. It should be noted that the truFreeze SCY system is currently approved for treatment of Barrett’s esophagus with low-grade dysplasia and high-grade dysplasia and malignancies. Therefore, SCY use in ESP management is considered off-label.

Previous studies suggested SCY as an effective option for treating mucosal cancer, which was not amenable to conventional treatment. There has been only 1 case report of ESP treated with SCY. Our patient underwent 3 sessions of SCY, and fourth surveillance endoscopy showed near-complete resolution. We believe that this case report has an important clinical implication regarding effective management of ESP, as cryotherapy is considered easy to use, minimally invasive, and has been associated with a low rate of complications and no hospital stay.

DISCLOSURES

Author contributions: M. Alomari acquired and analyzed the data and drafted the manuscript. V. Wadhwa reviewed the literature and drafted the manuscript. T. Erim critically revised the manuscript for important intellectual content, and is the article guarantor. P. Bejarano obtained histopathology slides. P. Amar performed follow-up endoscopies.
Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received April 5, 2018; Accepted December 21, 2018

REFERENCES

1. Sablich R, Benedetti G, Bignucolo S, Serraino D. Squamous cell papilloma of the esophagus report on 35 endoscopic cases. Endoscopy. 1988;20(1):5–7.
2. Narayani R, Young G. Recurrent proximal esophageal stricture associated with dysplasia in squamous cell papillomatosis. Gastrointest Endosc. 2002;56(4):591–4.
3. Kim E, Byrne MF, Donnellan F. Endoscopic mucosal resection of esophageal squamous papillomatosis. Can J Gastroenterol. 2009;23(6):415–9.
4. Attila T, Fu A, Gopinath N, Streutker C, Marcon N. Esophageal papillomatosis complicated by squamous cell carcinoma. Can J Gastroenterol. 2000;14(5):292–3.
5. Reynoso J, Davis R, Hemminger L, Krishna M, Woodward T. Photodynamic therapy and endoscopic metal stent placement for esophageal papillomatosis involving the entire esophagus. J Gastroenterol Hepatol. 2014;29(12):1951.
6. Tu R, Suryaprasad A, Prindiville T. Successful laser treatment of diffuse esophageal squamous papillomatosis causing dysphagia. Am J Gastroenterol. 2003;98:S193–4.
7. Pohl J. Extensive squamous papillomatosis of the esophagus. Z Gastroenterol. 2013;11(1):71–2.
8. Park S, Bang B, Kim H, Shin Y, Kim L. A case of esophageal squamous papillomatosis. Korean J Intern Med. 2012;27(2):243.
9. Corredine T, Bortniker E, Birk J. A rare cause of dysphagia: Squamous papillomatosis of the esophagus. Clin Gastroenterol Hepatol. 2016;14(3):A21–2.
10. Gençdal G, Değirmencioglu S, Akyldiz M. Diffuse esophageal squamous papillomatosis covering the entire esophagus. Clin Gastroenterol Hepatol. 2018;16(6):A28.
11. McDonald N, Amateau S. Treatment of diffuse esophageal squamous papillomatosis with cryotherapy. Am J Gastroenterol. 2016;111(10):1378.
12. Kibria R, Akram S, Moezzi J, Ali S. Esophageal squamous papillomatosis with dysplasia. Is there a role of balloon-based radiofrequency ablation therapy? Acta Gastroenterol Belg. 2009;72(3):373–6.
13. Takeshita K, Murata S, Mitsuji S, et al. Clinicopathological characteristics of esophageal squamous papillomas in Japanese patients—With comparison of findings from western countries. Acta Histochemica Cytochemica. 2006;39(1):23–30.
14. Franzin G, Musola R, Zamboni G, Nicolis A, Manfrini C, Fratton A. Squamous papillomas of the esophagus. Gastrointest Endosc. 1983;29(2):104–6.
15. Politoske E. Squamous papilloma of the esophagus associated with the human papillomavirus. Gastroenterology. 1992;102(2):668–73.
16. Syrjänen K, Pyrhönen S, Aukee S, Koskela E. Squamous cell papilloma of the esophagus: A tumour probably caused by human papilloma virus (HPV). Diagn Histopathol. 1982;5(4):291–6.
17. Szántó I, Szántó J, Banaí J, et al. Squamous papilloma of the esophagus: Clinical and pathological observations based on 172 papillomas in 155 patients. Orv Hetil. 2005;146:547–52.
18. Chang F, Janatuinen E, Pikkarainen P, Syrjänen S, Syrjänen K. Esophageal squamous cell papillomas failure to detect human papillomavirus DNA by in situ hybridization and polymerase chain reaction. Scand J Gastroenterol. 1991;26(5):535–43.
19. Reed P, Limauro D, Brodmerkel G, Agrawal R. Esophageal squamous papilloma associated with adenocarcinoma. Gastrointest Endosc. 1995;41(3):249–51.
20. Adler RH, Carberry DM, Ross CA. Papilloma of the esophagus: Association with hiatal hernia. J Thorac Surg. 1959;35:625–30.
21. Carr N, Bratthauer G, Lichy J, Taubenberger J, Monihan J, Sobin L. Squamous cell papillomas of the esophagus: A study of 23 lesions for human papillomavirus by in situ hybridization and polymerase chain reaction. Hum Pathol. 1994;25(5):536–40.
22. Fernández-Rodríguez CM, Badía-Figueroa N, Ruiz del Arbol L, Fernández-Seara J, Domínguez F, Avilés-Ruiz JE. Squamous papilloma of the esophagus: Report of six cases with long-term follow-up in four patients. Am J Gastroenterol. 1986;81:1059–62.
23. Benisch B, Mantell C. Multiple squamous papillomas of the esophagus. Arch Otolaryngol. 1974;100(5):379.
24. Kao P, Vecchio J, Schned L, Blazeky H. Esophageal squamous papillomatosis. Eur J Gastroenterol Hepatol. 2005;17(11):1233–7.

Copyright: © 2019 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American College of Gastroenterology. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.