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CASE REPORT | ENDOSCOPY

Effective Palliative Treatment of Obstructive Metastatic Esophageal Squamous Cell Carcinoma for Nearly 2 Years With Liquid Nitrogen Cryoablation Alone

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ABSTRACT

Esophageal squamous cell carcinoma (ESCC) often presents with debilitating dysphagia, significantly affecting quality of life. In metastatic disease, standard therapy with radiation and chemotherapy is associated with high morbidity. Liquid nitrogen cryotherapy offers a minimally invasive intervention for palliation in metastatic esophageal cancers. Although beneficial outcomes have been reported in esophageal adenocarcinoma, few studies have assessed its safety and efficacy as palliation treatment in metastatic ESCC. We present a case using endoscopic liquid nitrogen cryoablation alone as palliative therapy in a patient with obstructive metastatic ESCC resulting in persistent patent esophageal lumen 2 years after initiation of cryotherapy.

KEYWORDS: squamous cell carcinoma; cryoablation; esophagus

INTRODUCTION

Esophageal squamous cell carcinoma (ESCC) remains the most common type of esophageal cancer worldwide despite increasing rates of esophageal adenocarcinoma in Western populations.[1] ESCC often results from environmental exposure to toxins, including alcohol and tobacco. The chronic inflammation results in dysplastic changes and stratification of the squamous epithelial lining, which progresses to esophageal cancer. Patients with advanced or metastatic ESCC often present with symptoms of worsening dysphagia, chest pain, loss of appetite, and poor oral intake, with resultant malnutrition.

In patients with metastatic ESCC, the mainstay of symptomatic management includes radiation therapy, esophageal stenting, and surgical resection when indicated. Unfortunately, these interventions are often associated with complications, with surgical resection carrying a high morbidity of roughly 30%–50%.[2] While these interventions are the mainstay of therapeutic and palliative treatment, the impact on patient quality of life is significant.

Endoscopic cryotherapy has emerged over the past 15 years as a minimally invasive treatment of precancerous and malignant esophageal lesions. The administration of liquid nitrogen causes transient tissue ischemia and recruitment of immune cells resulting in localized tissue destruction.[3] Spray cryotherapy has been shown to be safe and effective in patients with esophageal adenocarcinoma with minimal adverse effects.[2] Preliminary studies have also demonstrated improvement in both dysphagia and quality of life in patients with esophageal cancer treated with cryotherapy.[4,5] However, more studies are needed to explore the combination of chemotherapy, radiation, cryotherapy, and resection of lesions with endoscopic or surgical intervention.

We present a case of utilization of liquid nitrogen cryotherapy for palliation of significant dysphagia in a patient with metastatic ESCC. It provides further evidence for the use of cryotherapy in patients for whom chemotherapy, radiation therapy, esophageal stenting, or surgical intervention is not indicated or unwanted.

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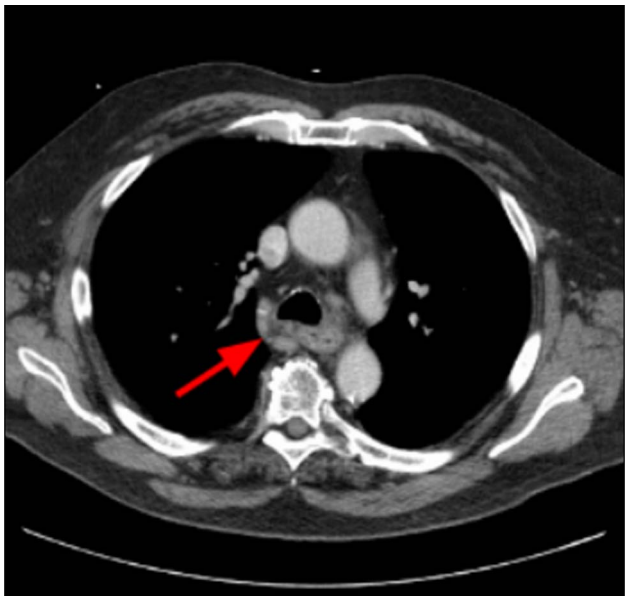

Figure 1. Chest CT with an irregular, circumferential esophageal mass (red arrow). CT, computed tomography.

CASE REPORT

Our patient is an 81-year-old man with a distant history of rectal cancer treated with partial distal colectomy presenting for intermittent chest pain that has progressed over 2 weeks and is worse with ingestion of solid foods. He has a 90-pack-year history of tobacco use with cessation 33 years before presentation and drinks 4–6 beers daily. Initial computed tomography revealed an irregular, circumferential mid-esophageal mass with mediastinal adenopathy concerning for malignancy (Figure 1). Upper endoscopy demonstrated a large, obstructing, fungating mass in the esophagus (Figure 2). Pathology was notable for invasive poorly differentiated ESCC (immunostaining positive for pancytokeratin and p40). Positron emission tomography confirmed metastatic disease (stage IVB, cT4 cN3 cM1, G3) involving the right lung and paraesophageal, mediastinal, supraclavicular, and right thoracic inlet lymph nodes (Figure 3).

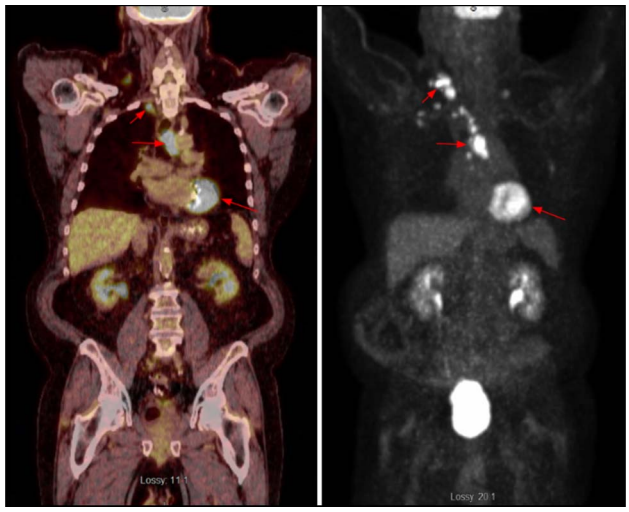

Figure 3. PET scan with uptake at the esophageal mass, mediastinal lymph nodes, and right lung nodule (red arrows). PET, positron emission tomography.

Given the diagnosis of metastatic ESCC, a multidisciplinary team including gastroenterology, thoracic surgery, radiology, pathology, medical oncology, and radiation oncology recommended palliative radiation, immunotherapy, and chemotherapy with pembrolizumab and mFOLFOX6, which he declined in favor of naturopathic treatments.

Over the subsequent 5-month period while pursuing other opinions and treatments, his dysphagia worsened and he continued to lose weight. While he continued to decline immunotherapy, chemotherapy, and radiation therapy, he was offered and agreed to endoscopic liquid nitrogen cryotherapy of the esophageal mass. He underwent 3 initial sessions over a 4-month span in 2-month intervals with a subsequent patent esophageal lumen (Figures 4–6). He

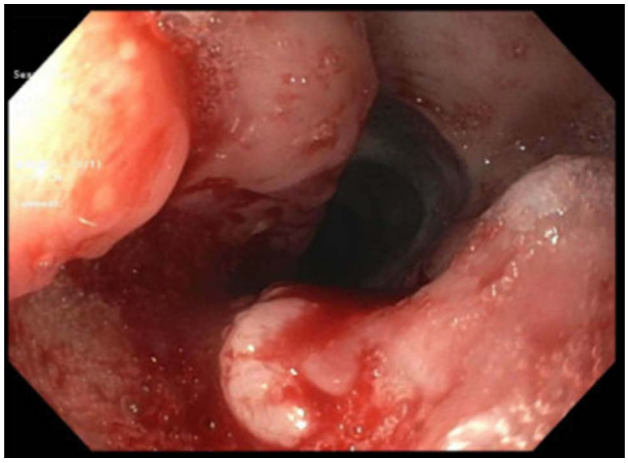

Figure 2. Initial upper endoscopic image with a large, partially obstructing esophageal mass.

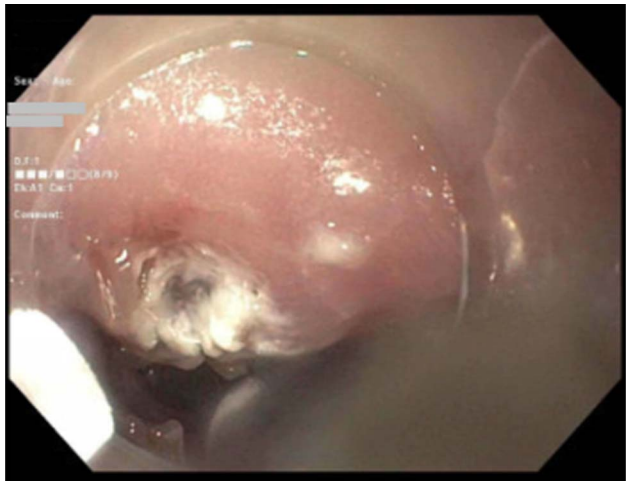

Figure 4. First endoscopic application of liquid nitrogen to the esophageal mass.

Figure 5. Small nodule remaining prior to third session of cryotherapy.

underwent additional cryotherapy sessions for mild residual mucosal abnormalities 2 months (Figure 7), 8 months (Figure 8), and 13 months (Figure 9) after his initial 3 cryotherapy sessions. At his most recent follow-up endoscopy 22 months after initiation of cryotherapy (18 months after completion of his initial 3 cryotherapy sessions), endoscopy revealed a patent lumen with minimal residual disease (Figure 10). He tolerated all cryoablation sessions without complications, with resolution of dysphagia, improved oral intake, and stable weight.

DISCUSSION

To date, this is the longest published case of clinical remission achieved in a patient with obstructive metastatic ESCC with the use of palliation cryotherapy alone. This patient is nearly 2 years out from initiation of liquid nitrogen therapy with a patent esophageal lumen and resolved dysphagia.

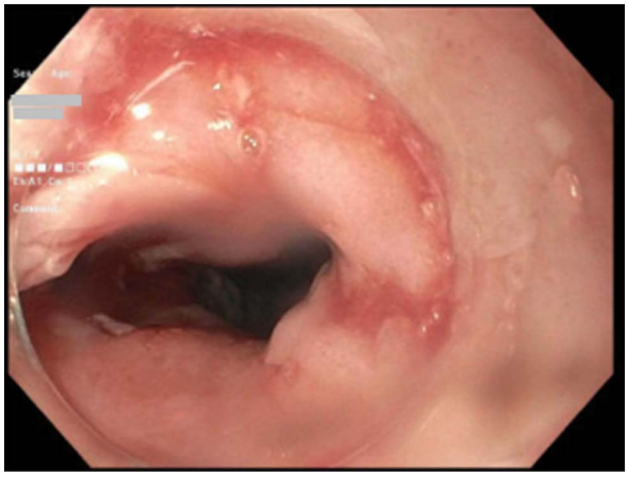

Figure 6. Final image after completion of the third cryotherapy session.

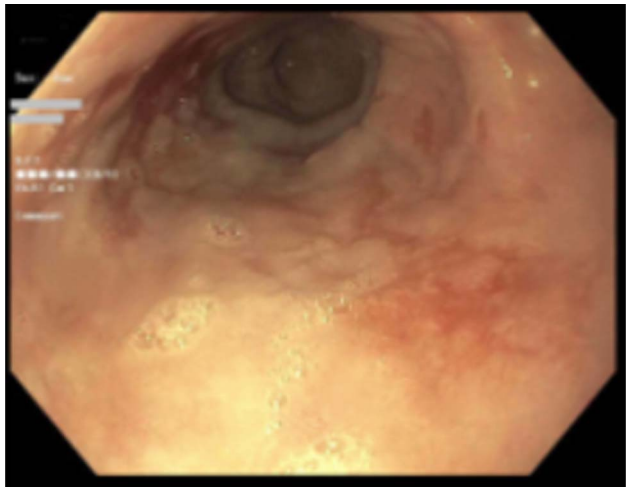

Figure 7. Subsequent cryoablation for minimal residual disease in initial 3 cryotherapy sessions.

Patients with advanced esophageal cancer can present with significant chest pain, dysphagia, and, in severe cases, esophageal obstruction. Such symptoms can significantly affect a person's quality of life. Previous studies have highlighted the effectiveness of cryoablation in improving dysphagia and quality of life in symptomatic patients.

This was first demonstrated in a case report by Cash et al[6] where spray cryotherapy was well tolerated in a patient with ESCC with improved dysphagia. In a recently published abstract by Kachaamy et al,[4] 35 patients with inoperable esophageal cancer underwent cryotherapy and were found to have improved quality of life and dysphagia scores. In a case series by Kachaamy et al[5] evaluating the use of liquid nitrogen cryotherapy in 49 patients with inoperable esophageal cancer, cryotherapy treatments were associated with significant improvement in patient-reported severity of dysphagia. These

Figure 8. Subsequent cryoablation for minimal residual disease at 8 months after initial 3 cryotherapy sessions.

Figure 9. Subsequent cryoablation for minimal residual disease at 13 months after initial 3 cryotherapy sessions.

studies demonstrate how spray cryotherapy can offer an effective, minimally invasive intervention in patients who are not surgical candidates.

Tolerability to treatment is another component of spray cryotherapy that suggests that it would be a more preferable palliative treatment in patients with advanced disease in comparison with chemotherapy, radiation therapy, and surgical resection. A multicenter study conducted by Solomon et al[7] found that compared with liquid nitrogen spray, patients with Barrett's esophagus receiving radiofrequency ablation were 5 times more likely to experience postprocedural pain.

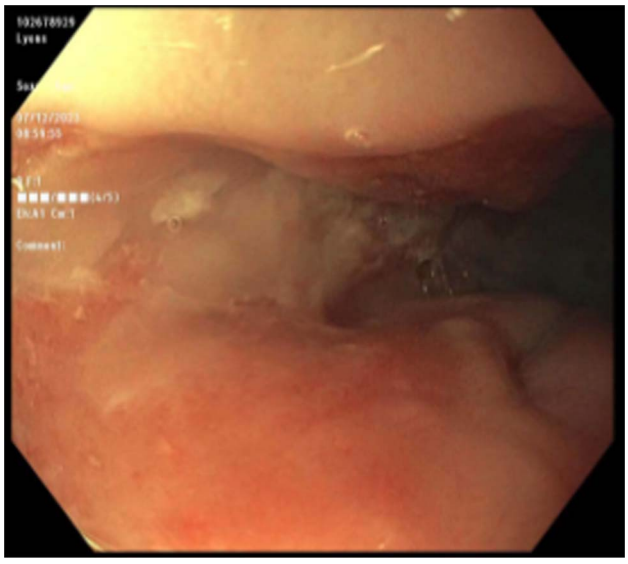

Figure 10. Subsequent cryoablation for minimal residual disease 18 months after initial 3 cryotherapy sessions (22 months after the initial cryotherapy session).

Furthermore, in the case series by Kachaamy et al[5] mentioned above, improvements in dysphagia were only associated with minimal mild adverse events (5%) and 1 case of perforation secondary to dilation before cryotherapy. These studies suggest that spray cryotherapy has good tolerability and is associated with minimal adverse effects.

Spray cryotherapy has also demonstrated positive results in achieving remission in patients with ESCC. This was demonstrated in a prospective study conducted using endoscopic balloon ablation in patients with histologic moderate to high-grade squamous cell neoplasia of the esophagus, reported 97% of patients (study population of 80 patients) had complete neoplastic remission at 12 months with a median of 1 treatment of endoscopic cryoballoon ablation.[8]

Palliative endoscopic esophageal stenting is a well-established, noninvasive, endoscopic intervention used for palliation of dysphagia in esophageal cancer. Studies have demonstrated improvements in both dysphagia and quality of life in patients with esophageal cancer who underwent esophageal stenting.[9–11] Table 1 summarizes the outcomes and major adverse events across different studies in which palliative esophageal stenting and palliative endoscopic cryotherapy were used for inoperable esophageal cancer. While both palliative cryotherapy and esophageal stenting resulted in improvements in dysphagia and quality of life, cryotherapy seems to be associated with less frequent major adverse events.

This case report provides endoscopic evidence of cryoablation's ability to reduce tumor burden and achieve local control in ESCC. Cryoablation alone seems to be a safe, effective, and well-tolerated palliative treatment for patients with metastatic ESCC. Further larger scale studies are needed to confirm the benefit of cryotherapy in patients with ESCC.

DISCLOSURES

Author contributions: D. Aintabi: responsible for supervision, design of case report, collection of case information, writing original draft, critical reviewing and editing, publication of case report, approval of final publication. A. Saliares: responsible for reviewing and editing, collection of case information, approval of final publication. E. Berinstein: responsible for critical reviewing and editing, approval of final publication. N. Gunaratnam: responsible for supervision, design of case report, reviewing and editing, approval of final publication.

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Previous presentation: This case report was presented by Daniel Aintabi at the American College of Gastroenterology Annual Scientific Meeting; October 2022; Charlotte, NC. AJG: S2846 Liquid Nitrogen Cryoablation Alone Is an Effective

Table 1. Comparison table of outcomes and major adverse events with palliative endoscopic cryotherapy and esophageal stenting

Study	No. of patients (by sex)	No. of patients by histologic type and staging of cancer	Intervention	No. of patients and type of major adverse events	No. of intervention related deaths	Summary of results
Kachaamy et al[5] (2018)	49 patients (39 male, 10 female)	Type: 47 EAC, 2 ESCC Stage: 8 stage III and 41 stage IV	Palliative cryotherapy	1 EP with dilation before cryotherapy, 1 benign stricture	None	Improved mean dysphagia score from 2.4 to 1.7 with cryotherapy ($P < 0.001$)
Kachaamy et al[4] (2022)	35 patients (29 male and 6 female)	Type: unspecified Stage: 5 stage III and 30 stage IV	Palliative cryotherapy	3 (unspecified type of complication)	None	EORTC QLQ-OES18 questionnaire QoL score improved from 35.9 to 29.8 after 3 cryotherapy sessions ($P = 0.001$) Mean dysphagia score improved from 1.97 to 1.25 after cryotherapy ($P = 0.004$)
W□odarczy and Kuzdal (2018)[9]	442 patients (379 male, 63 female)	Type: 311 ESCC, 111 esophagogastric junction (histology unspecified) Staging: unspecified	Palliative esophageal stenting	6 esophageal bleeds requiring blood products, 4 EP after dilation, 4 airway compression from stenting (3 requiring mechanical ventilation), 18 stent migrations, 55 stent obliteration by ingrowing tumor, 34 patients with TEF (15 TEF after stenting, 19 with TEF at presentation)	2 deaths (1 perforation, 1 arrhythmia after stenting)	Improved mean dysphagia grading score (4 point grade scale from 0 to 3) from 3.0 to 1.0 after stenting ($P = 0.00001$)
Madhusudhan et al[10] (2009)	33 patients (22 male, 11 female)	Type:, 27 ESCC, 27 EAC, 1 small cell carcinoma Staging: unspecified (13 locally advanced, 20 metastatic)	Palliative esophageal stenting	5 for stent obstruction, 2 stent migration	None	Improved and sustained EORTC QLQ-OES18 questionnaire dysphagia scores from 16.5 to 91.6 1-week post-stenting, 90.6 2-months post-stenting ($P < 0.01$)
Kujawski et al[12] (2012)	46 patients (41 male and 5 female)	Type: unspecified Staging: unspecified	Palliative esophageal stenting	1 respiratory tract compression, 3 EP, 1 TEF, 1 stent malpositioning, 2 stent migrations, 2 stent occlusions	1 death	Assessment of safety profile of palliative esophageal stenting
Schauer et al[11] (2021)	40 patients (29 male, 11 female)	Type: 27 EAC, 11 SCC, 2 other subtypes Staging: unspecified	Palliative esophageal stenting	2 esophageal bleeding, 4 stent migrations	None	Improved EORTC QLQ-C30 questionnaire overall global QoL score (mean 35 to 46, $P = 0.01$) 1 month after esophageal stenting Improved EORTC OES-18 questionnaire dysphagia scores from 65.8 to 35.1 ($P < 0.01$) 1 month after stenting

EAC, esophageal adenocarcinoma; EP, esophageal perforation; ESCC, esophageal squamous cell carcinoma; QoL, quality of life; TEF, tracheoesophageal fistula.

Palliative Treatment for Metastatic Esophageal Squamous Cell Carcinoma.

Informed consent was obtained for this case report.

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