

Management of Early-Stage Esophageal Adenocarcinoma by Endoscopic Spray Cryotherapy in the Setting of Portal Hypertension With Varices

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ABSTRACT

The use of endoscopic spray cryotherapy to manage pathological conditions of the esophagus has become increasingly common. This mucosal ablation technique is believed to carry a lower risk of bleeding than other modalities. A 71-year-old woman and a 64-year-old man with portal hypertension and varices were diagnosed with invasive esophageal adenocarcinoma during routine variceal surveillance. Staging by endoscopic ultrasound and computed tomography was uT1N0M0 in both patients. They each underwent mucosal ablation using liquid nitrogen cryosprays with no adverse events. Both cancers completely resolved with 2 treatments, and neither patient has shown recurrence of neoplasia during follow-up observations for up to 2 years.

INTRODUCTION

Barrett's esophagus (BE) is characterized by intestinal metaplasia arising from the squamous epithelium of the esophagus. This may progress to low-grade dysplasia and high-grade dysplasia, both of which elevate the risk of progression to malignancy.¹ BE has thus been identified as the major risk factor for esophageal adenocarcinoma, which involves the formation of malignant tumors from dysplastic BE tissue.² Detection of both dysplastic BE and malignant neoplasms has been steadily climbing in the United States and other Western countries.² Currently, there are multiple management options available for BE, including long-term surveillance of nondysplastic segments of the transformed esophageal mucosa, surgical esophagectomy, endoscopic mucosal resection, and mucosal ablation.^{1,3} Portal hypertension is a frequent complication of hepatic cirrhosis. It arises from the increased vascular resistance of the cirrhotic liver and can lead to increased production of vasodilators and extensive angiogenesis within the portal venous system.^{4,5} These, in turn, can promote the development of both gastric and esophageal varices.⁴ Patients who develop large gastroesophageal varices may be at increased risk for spontaneous gastroesophageal hemorrhaging, which can be fatal. Thrombocytopenia also develops with worsening portal hypertension. It is recommended that patients with suspected cirrhosis and varices receive routine endoscopic variceal surveillance so that preventative measures against bleeding, such as pharmacological treatment or band ligation, can be performed.^{6,7}

CASE REPORT

At our clinic and others, spray cryotherapy is an available option for endoscopic treatment in which liquid nitrogen cryosprays, delivered through a specialized cryocatheter in brief repeated cycles, can ablate dysplastic or cancerous tissue by causing rapid freezing, gradual thawing, and subsequent necrosis of cells in the treated area.³ This therapy was first used in the management of BE and has already been demonstrated to be safe and effective in cases of early-stage esophageal cancer in which the subject was medically ineligible for other interventions or was receiving cryotherapy in conjunction with other modalities.^{3,8} It is believed to carry a lower risk for bleeding than other modalities because of the mechanism by which it induces necrosis, which involves significant vascular thrombosis and circulatory stasis.⁹ It is further hypothesized that low-pressure liquid nitrogen cryospray is



Figure 1. (A) Ulcerated nodular lesion in the esophagus, (B) liquid nitrogen cryospray treatment, and (C) resolution of the lesion after 2 months.

less invasive than other modalities in that it does not cause significant damage to the scaffolding provided by the extracellular matrix, facilitating repopulation by surrounding healthy tissue after treatment.⁹

Patient 1: A 71-year-old woman with a medical history of hepatitis C with cirrhosis and portal hypertension was undergoing endoscopic variceal surveillance when a small, ulcerated, nodular lesion was found in the distal esophagus. Biopsies of the lesion and surrounding tissue confirmed a diagnosis of invasive adenocarcinoma in a background of BE. Endoscopic ultrasound (EUS) staging found the tumor to be stage uT1N0M0. EUS also confirmed the presence of extensive gastric and esophageal varices. Endoscopic mucosal resection and radiofrequency ablation treatment options were discussed with the patient but were believed to carry a high risk of bleeding from the varices and thrombocytopenia. The patient has a platelet count of 72,000, a Model for End Stage Liver Disease score of 16, and a normal international normalized ratio of 1.0. The patient elected to undergo liquid nitrogen spray cryotherapy. The tumor site was treated with two 30-second cycles of liquid nitrogen cryosprays with good effect. This number and duration of cryospray treatment is used for all cancer patients at this institution who undergo this therapy.³ A follow-up endoscopy 2 months later showed complete resolution of the lesion (Figure 1). The patient has shown no recurrence of neoplasia

in over 24 months of follow-up. There was no bleeding or other adverse events.

Patient 2: A 64-year-old man with hepatitis C virus-related cirrhosis and known portal hypertension was found to have a new, small, nodular lesion at the gastroesophageal junction during a surveillance endoscopy. Biopsies of the lesion confirmed invasive adenocarcinoma in the setting of short-segment Barrett's mucosa. Computed tomography and EUS staging demonstrated the lesion to be a uT1N0M0 carcinoma. His esophageal varices were small but his platelet count was less than 40,000, his Model for End Stage Liver Disease score was 9, and his international normalized ratio was elevated at 1.2. After a review of the options, the patient elected to undergo spray cryotherapy. After 2 30-second cycles of liquid nitrogen cryospray treatment, the lesion was completely ablated (Figure 2). This number and duration of cryospray treatment are used for all cancer patients at this institution who undergo this therapy.³ After 1 year of surveillance, there has been no endoscopic recurrence of neoplasia. There was no bleeding or other adverse events.

DISCUSSION

Cases involving the use of liquid nitrogen spray cryotherapy in the management of esophageal adenocarcinoma in high-risk patients, such as those with esophageal varices and/or



Figure 2. (A) Small nodular lesion at the gastroesophageal junction, (B) liquid nitrogen cryospray treatment, and (C) no recurrence of neoplasia after 1 year.

thrombocytopenia, have not been frequently reported in the past. The results and patient outcomes reported here support that this treatment is a safe and effective technique for the management of early-stage esophageal cancer in patients with portal hypertension, varices, and thrombocytopenia. Despite recent advances in its management, variceal bleeding remains one of the most important complications of hepatic cirrhosis because of its frequency and high mortality rate.¹⁰ The increased bleeding risk presented by gastroesophageal varices and thrombocytopenia is a critical consideration for patients in need of any endoscopic or surgical intervention in conditions affecting the stomach or esophagus, especially esophagectomy.¹¹

Endoscopic therapy has been more favorable over esophagectomy in recent years for this reason, among others.³ Spray cryotherapy is of particular importance in this respect because it does not cause mechanical injury to targeted tissues and surrounding vasculature; instead, cycles of rapid freezing and gradual thawing of the treated area cause the initial formation of abrasive intracellular ice crystals and disruption of cytosolic solute homeostasis, in addition to temporary hemostasis and progressive thrombosis in the local vasculature.⁹ This is marked by the formation of a cryogenic lesion slightly smaller than the site of initial cryogenic injury, followed by visible necrosis of the affected tissue within 2 days.¹² The cases presented provide strong clinical examples of spray cryotherapy procedures in which bleeding complications were avoided, possibly because of the intrinsically hemostatic mechanism of cryogenic injury.

Now that patients with hepatitis C virus-related cirrhosis and portal hypertension are living longer, endoscopic surveillance will likely uncover more comorbid cases of BE and neoplasia of the esophagus.¹³ The optimal therapy for these high-risk patients has not been determined, but we present 2 who have had safe and successful eradication of adenocarcinoma using spray cryotherapy alone. Although other examples of positive long-term outcomes for patients who undergo spray cryotherapy in various other settings exist, further studies are required to determine whether it is the preferred modality in patients requiring endoscopic treatment for significant mucosal lesions who are at risk for bleeding from varices and thrombocytopenia.¹⁴

DISCLOSURES

Author contributions: WJ Coyle revised the manuscript and is the article guarantor. EA Pillsbury wrote the manuscript.

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