

Cryotherapy for Two Cases of Recurrent Laryngeal Papillomas*

Joon Kyoo Lee, MD, PhD, Dong Hoon Lee, MD

Department of Otorhinolaryngology-Head and Neck Surgery, Chonnam National University Medical School and
Chonnam National University, Hwasun Hospital, Hwasun, Korea

재발성 성문부 유두종 환자의 냉동치료*

전남대학교 의과대학 화순전남대학교병원 이비인후-두경부외과학교실

이 준 규 · 이 동 훈

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목 적

액체 질소를 이용한 냉동 치료는 피부 사마귀 치료에 널리 사용되어왔다. 본 연구에서는 재발성 성문부 유두종 환자에 대해 냉동 치료를 시행하여 그 치료 결과를 알아보고자 하였다.

방 법

냉동치료 전에 재발성 유두종으로 확진 되었고, 다른 호흡기에는 병변이 없었던 환자를 대상으로 하였다.

결 과

냉동 치료의 국소적, 전신적 합병증 및 부작용은 없었다. 그러나, 성문부 유두종은 냉동 치료 후 각각 3개월과 2년 후에 재발하였다.

결 론

냉동치료는 초기에는 성문부 유두종 병변의 치료에 효과가 있으나, 장기적인 효과는 떨어졌다. 향후 더 많은 증례와 추적관찰이 필요할 것으로 생각된다.

중심 단어 : 냉동치료 · 후두 · 유두종.

Introduction

Laryngeal papilloma causes devastating lesions leading to serious clinical conditions(severe dysphonia, or laryngeal dyspnea).^{1,2)} The mechanism underlying acquisition and trans-

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교신저자 : 이동훈, 519-809 전남 화순군 화순읍 일심리 160
전남대학교 의과대학 화순전남대학교병원 이비인후-두경부외과학교실

전화 : (061) 379-8190 · 전송 : (061) 379-7761

E-mail : leen3l@hanmail.net

mission of laryngeal papillomas has not been determined. Recurrence of laryngeal papillomas after excisional therapy is common and repeated surgery causes additional vocal cord scarring. Medical management of laryngeal papillomas, including administration of interferon and indole-3-carbinol, has been generally unsuccessful.³⁾ Recently, intralesional cidofovir injection and/or removal of laryngeal papillomas have been reported to be effective.³⁻⁵⁾ However, these methods need to be repeated at monthly intervals.

Cryotherapy with liquid nitrogen is widely used for to treat cutaneous warts in primary care practices.⁶⁾ Therefore, we used cryotherapy with liquid nitrogen to treat two patients with vocal cord papillomas using a medical device specifically designed for laryngeal lesions.

Patients and Methods

1. Patient

This study was approved by the Chonnam National University Hospital Ethics Committee. Informed consent was obtained for both patients enrolled in the study. Entrance criteria included a minimum age of 18 years, the presence of papillomas limited to the glottis as determined by biopsy, and no evidence of other disease within the tracheobronchial tree.

1) Patient 1

A 48-year old male visited Chonnam national university hospital after experiencing hoarseness for 6 months. He complained about sensing a lump in his throat and had a habit of clearing his throat due to the foreign body sensation. He had quit smoking 3 years ago and had a prior 30-year history of smoking. Flexible laryngoscopy found multiple recurring papillomatous masses on the bilateral false vocal cord and true vocal cord that extended into the anterior commissure after the patient underwent two conventional endoscopic pro-

cedures(4 and 9 months prior to the study) to remove the tumors(Fig. 1A).

2) Patient 2

A 37-year old male visited Chonnam national university hospital for hoarseness lasting for 3 months. He had suffered from hepatitis B and was a current smoker with a 20-year history of tobacco use. The patient's occupation made him abuse his voice. The patient has undergone suspension laryngoscopy to remove laryngeal papillomas 7 months prior to the study. Flexible laryngoscopy showed recurrence of papilloma on the bilateral true vocal cord and left false cord(Fig. 2A).

2. Methods

We purchased a Cryo Surgery System(Cortex Technology ; Denmark). Shown in Fig. 3, this device consisted of two units : a Cryo-gun and Probe. The Cryo-gun(CryoPro-Maxi ; Cortex Technology) can hold up to 500mL of liquid nitrogen(-196°C). It was 11.1×2.67 inches in size and had an operating pressure of 10 ± 2 Pascal. The use of this unit was approved by Korean Food and Drug Association. The Probe was designed spe-

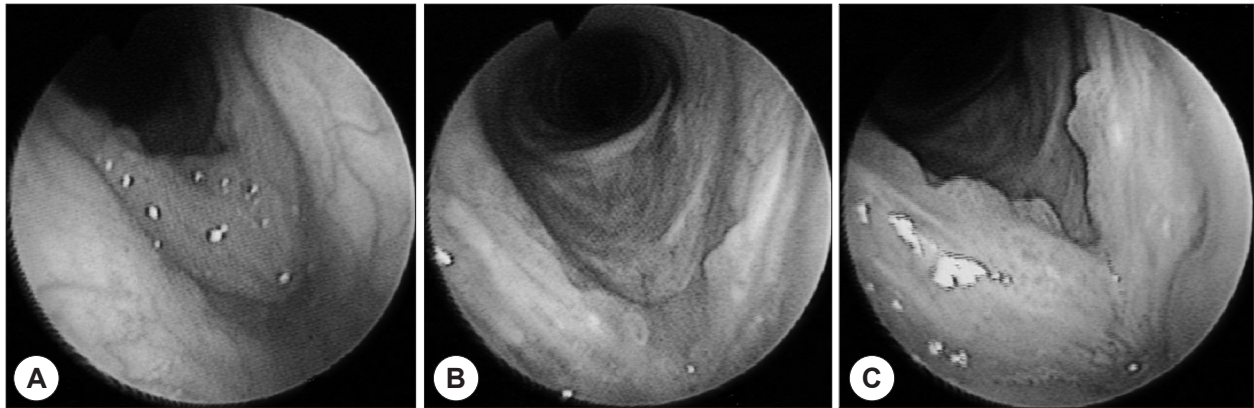


Fig. 1. In patient 1, flexible laryngoscopy found multiple papillomatous masses on the bilateral false vocal cord and true vocal cord(A). At the 1-month follow-up after cryosurgery, the papilloma on the bilateral false cord disappeared and the one on the bilateral true vocal cord decreased in size(B). The lesions on both true vocal cords had increased in size at the 3-month follow-up(C).

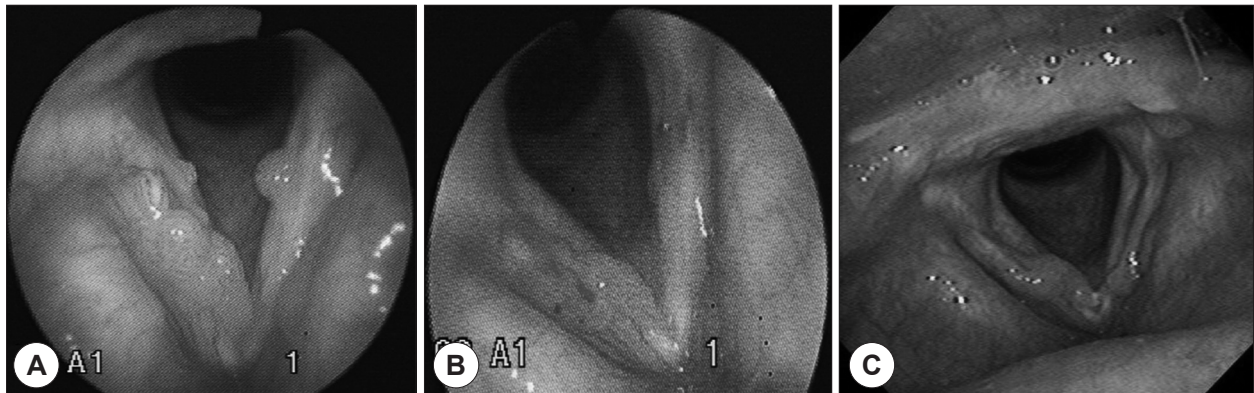


Fig. 2. In patient 2, flexible laryngoscopy found papilloma recurrence on the bilateral true vocal cord and left false cord(A). The papilloma on the left true vocal cord disappeared and the one on the right true vocal cord decreased in size 1 month after surgery(B). The lesions on both true vocal cords were slightly increased in size after 2 years(C).

cifically for treating laryngeal lesions. It contains a long bar 250mm in size and a tip 1mm in size(point of papilloma contact) at the end of the bar.

Cryotherapy was performed during the suspension laryngoscopy with the patient under the general anesthesia and endotracheal intubation. When the handle of the Cryo-gun was pressed, liquid nitrogen was sucked out of the container, traveled through inside of the long bar, and cold energy was immediately delivered to the sharp tip in the end. The tip was in direct contact with the laryngeal papilloma for about 3-5 seconds until the size of the mass was reduced by the cold(Fig. 4). The vapor that escaped during surgery was immediately evacuated by the suction device.

Cryotherapy was not performed on lesion in the anterior commissure to avoid postoperative formation of a glottic web in patient 1. Excisional treatment was not performed in the current study.

Results

No adverse reactions, including additional laryngeal scar-

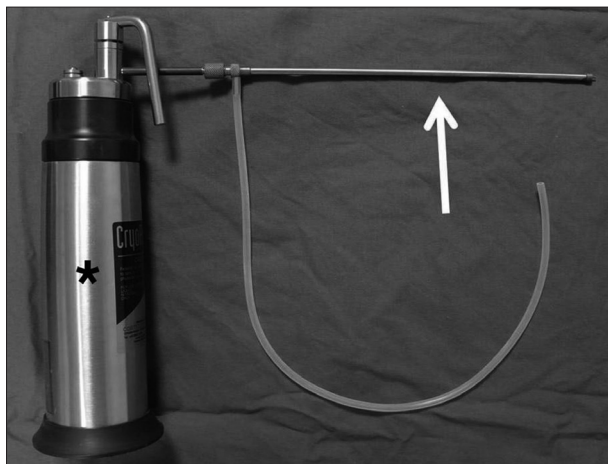


Fig. 3. The photograph shows the Cryo Surgery System that consists of two units : the Cryo-gun(asterisk) and Probe(arrow).

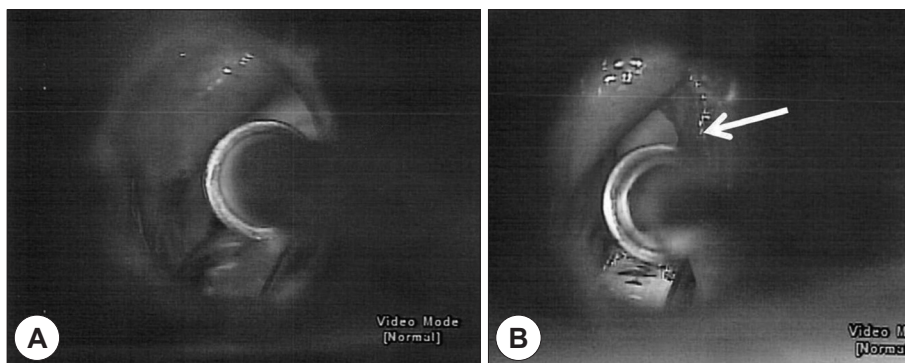


Fig. 4. Cryosurgery was performed with the suspension laryngoscopy(A). The tip was in direct contact with the lesion on the right true vocal cord(arrow, B).

ring or systemic toxicity, were observed after treatment. Both patients were discharged from the hospital on the first post-operative day. They were instructed not to irritate the vocal cord and to drink water about 3 or 4 liters per day.

Patient 1 visited the hospital 1 month after cryotherapy. The papilloma on the bilateral false cord had disappeared and that the one the bilateral true vocal cord had decreased in size (Fig. 1B). However, the lesions on both true vocal cords had increased in size at the 3-month follow-up(Fig. 1C). The patient was transferred to another hospital and underwent papilloma removal with a LASER. In response to a phone questionnaire, he stated that his voice was in relatively good condition.

Patient 2 visited the hospital 1 month after cryotherapy. The papilloma on the left true vocal cord had disappeared and the one the right true vocal cord had decreased in size (Fig. 2B). The patient's voice had improved. He was lost during follow-up until 2 years had passed because he did not complain of any vocal problem. However, lesions on both true vocal cords had slightly increased in size at the 2-year follow-up(Fig. 2C). The patient stated that he did not wish to undergo further surgery and was followed-up with observation.

Discussion

The symptoms of laryngeal papillomas are hoarseness, dysphonia, stridor, and subsequent respiratory distress. Although the lesions are more commonly observed during infancy and childhood, they frequently occur during adulthood at which time they are less aggressive and associated with slower recurrence. Laryngeal papillomas appear predominantly in males.

The tendency for regression at puberty and adult male predominance suggests that a hormonal factor influences laryngeal papilloma etiology. A viral origin seems to be the most plausible cause of this disease. In particular, a frequent asso-

ciation of skin warts, which are known to be caused by viruses, and papillomas of the pharynx and larynx has been noted.⁷⁾

Most medical approaches to treat papillomas of the larynx have been discarded as the results of these procedures were equivocal. Bielamowicz *et al.*³⁾ reported that intralesional injection of cidofovir (an antiviral agent) is an excellent treatment option associated with limited local and systemic toxicities. However, in this study, subjects received monthly injections of cidofovir that were repeated until no papillomas could be visually identified during intraoperative evaluation. On average, six injections were required to achieve remission. Two other studies reported that intralesional injection of cidofovir was effective.^{4,5)} However, in these studies, cidofovir was given to the patients on a monthly basis after the papilloma was surgically or endoscopically (CO₂ laser) excised.

Other methods for treating laryngeal papillomas include surgical removal and destruction by a CO₂ or 585-nm pulsed dye laser.⁸⁻¹⁰⁾ However, these techniques are not perfect. Patients presented with recurrences after first surgical treatment,⁸⁾ disease involution but remained,⁹⁾ and less effective in the management of exophytic lesions because of its limited depth of penetration.¹⁰⁾

The use of cryotherapy of treating laryngeal papillomas was first reported in 1960.¹¹⁾ The development of an apparatus using liquid nitrogen in a closed system capable of producing rapid, readily controllable temperature changes from 30 to -196°C made cryosurgical techniques practical.¹²⁾ However, studies using cryotherapy for laryngeal papilloma have not been reported in the English literature from the 1980's to 2010⁷⁾.

Cryotherapy induces skin and vascular damage, leading to both epidermal and dermal cellular necrosis.¹³⁾ Freezing results in tissue destruction by physically rupturing cell membranes, dehydration from toxic concentrations of electrolytes, vascular stasis, and denaturation of protein molecules.¹⁴⁾ When living tissue is cooled to just below -20°C, ice crystals form an ice ball, and as the temperature is lowered, the ice ball spreads. There is a sharp line of demarcation at the edge of the ice ball, and the effect of the cold is limited to tissues covered by the ice ball. Necrosis takes place, and within 2 to 4 weeks the necrotic tissue is sloughing. Inflammation is virtually absent in the surrounding tissues with minimal scarring and fibrosis. After the sloughing is complete, re-epithelization occurs resulting in the restoration of normal respiratory epithelium.

Cryotherapy has been used successfully to treat papillomas of the skin. Singleton and Adkins hypothesize that if skin

warts and papillomas of the pharynx and larynx are both caused by a virus, possibly even the same virus, then it is logical to expect that cryotherapy will produce good results for the treatment of this condition.¹²⁾ Since cryotherapy results in minimal fibrosis and scarring and permits rapid resurfacing with normal respiratory epithelium, this technique is an ideal procedure for use in the larynx and tracheobronchial tree.

In this study, cryotherapy seemed to be initially effective, especially within a month after the procedure. However, this method failed to produce long-term curative effects. Similar to other studies,³⁻⁵⁾ repetitive cryotherapy procedures performed on a monthly basis after the initial removal of laryngeal papillomas were hypothesized to be more effective. Bruggink *et al.*⁶⁾ also reported that liquid nitrogen cryotherapy performed every two weeks was the most effective therapy for treating common warts.

In summary, we attempted to use cryotherapy with liquid nitrogen to treat two patients with recurrent vocal papillomas using a medical device specifically designed for this type of surgical procedure. The cryotherapy seemed to be effective based on observation made 1 month surgery. However, the lesions recurred 3 months and 2 years after the cryotherapy in both patients. Further studies are required in order to provide the safety and effectiveness of cryotherapy for laryngeal papilloma.

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