



Research Article

CRYOTHERAPY AS AN EFFECTIVE ALTERNATIVE FOR THE MANAGEMENT OF VERRUCOUS HYPERPLASIA LESION- A CASE REPORT

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ABSTRACT

Verrucous hyperplasia is a histopathological entity, which shows considerable clinical and histopathological resemblance to verrucous carcinoma. The treatment plan originally included surgery, chemotherapy, radiation, or a combination. This case report describes an adjuvant treatment method, simple cryosurgery, which offers satisfactory results. Cryotherapy is the deliberate destruction of tissue by the application of extreme cold. Liquid nitrogen is the universal freezing source because of its low boiling point. Various methods have been devised for the use of cryotherapy. They include the spray freeze technique, the applicator technique, the cryoprobe method, and the thermos-coupler method. The advantages of the present technique are easy to use, very low morbidity, limited postoperative care, no sophisticated equipment required, and most of all satisfactory results.

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INTRODUCTION

Verrucous hyperplasia is a histopathological entity, which shows considerable clinical and histopathological resemblance to verrucous carcinoma. This was initially described by Shear and Pindborg (1980) and differentiated from verrucous carcinoma. They separated these entities based on the lack of invasive growth in the verrucous hyperplasia that is entirely superficial to adjacent normal epithelium. Verrucous hyperplasia is not only encountered in oral mucosa but also sinonasal and laryngeal mucosa.<sup>1</sup>

Verrucous hyperplasia is a premalignant exophytic oral mucosal lesion with a predominantly verrucous or papillary surface; this lesion can subsequently transform into verrucous carcinoma. Cryosurgery is performed using a cryogen including liquid nitrogen, nitrous oxide carbon dioxide gas and other compressed gases, but the most common cryogen by far is liquid nitrogen to cool the targeted tissue to subzero temperatures.<sup>2</sup>

The treatment plan originally included surgery, chemotherapy, radiation, or a combination. In only surgery or with radiation treatment lesion shows a high recurrence rate. Surgery has been used widely; however, those with wide involvement often make total excision difficult. This article describes a simple and effective treatment method, simple cryosurgery, which offers satisfactory results without resorting to complicated surgery and/or the use of sophisticated equipment.<sup>2</sup>

We are reporting a case describing verrucous hyperplasia with a lateral border of the tongue.

CASE REPORT

A patient aged 35 years old male came to the Department of Oral and Maxillofacial Surgery, with a chief complaint of reduced mouth opening and whitish growth on the left lateral border of the tongue since 1 year. Past medical, dental, and family history were not contributory. The patient had a history of tobacco chewing 4-5 times a day and a history of smoking and alcohol consumption for 20 years, patient has quit his habit for the last 5 months. On clinical examination, there was whitish lesion present at the left lateral border of the tongue which was approximately 3\*2 cm, and it was extending anteroposteriorly from 34 to 37 region of the left lateral border of the tongue. It appeared as a single, well-circumscribed lesion. It was non-tender, non-scrapable, did not disappear on stretching, and had clearly defined borders and a rough surface. We also noticed reduced mouth opening and blanching on the left buccal mucosa and reduced tongue protrusive capacity. Vertical bands were palpable on both the right and left buccal mucosa.

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a: Patient's profile photograph



e 1 week follow up



b Preoperative



f 3 month follow up



c Intraoperative



d Immediate Postoperative

The lesion was extensive so first, we planned for an incisional biopsy. The incisional biopsy was done. The report of incisional biopsy was suggestive of verrucous hyperplasia. Then the patient was planned for cryotherapy. A signed informed consent was taken from the patient for the surgical intervention. Considering his apprehension and treatment benefits, cryosurgery was performed. Local anesthesia (2 % lignocaine, 1:80,000 adrenaline) was given to anesthetize the surrounding structures. A closed system consisting of a cryoprobe, and nitrous oxide gas was used. Nitrous oxide was released from high pressure inside the cryotip which was placed directly on the lesion. The lesion was exposed directly to three consecutive "freeze-thaw cycles" and each cycle lasted for 5-10 sec. The cryoprobe was moved from the center of the lesion to the borders until the lesion appeared white and frozen, resembling an ice ball. Fig d shows the appearance of the lesion immediately after treatment, at 1 week follow up (fig e). The clinical outcome was satisfactory at 3 months follow-up (fig f). The patient is now on periodic evaluation and doing well.

## DISCUSSION

Verrucous hyperplasia is a morphological variant of verrucous carcinoma by Sloomwage J P and Muller H (1983).<sup>3</sup> Essential features in distinguishing verrucous hyperplasia from verrucous carcinoma is the location of the thickened epithelium concerning adjacent normal appearing epithelium. In verrucous hyperplasia, most of the hyperplastic broadened rete ridges lay above the adjacent normal epithelium while verrucous carcinoma on the contrary exhibits a downward growth pattern of otherwise similar rete ridges also according to shear and Pindborg JJ (1980) stated that verrucous carcinoma often retracts normal epithelium down with them

into underlying connective tissue. For that distinction, the biopsy must include adjacent normal epithelium.<sup>1</sup>

Cryotherapy is the deliberate destruction of tissue by the application of extreme cold.<sup>4</sup> The origin of the word cryotherapy lies in the Greek Word "kryos" which means "to frost".<sup>5</sup> Cryotherapy, also known as cryosurgery, can be described as a therapeutic modality that utilizes the application of low temperatures for the deliberate destruction of tissue structure.

Cryosurgery uses freezing temperatures to achieve specific effects on tissues. It has been used as the treatment of choice, as an alternative method, or as an adjunct to other methods for diverse benign and malignant lesions. The significance of cryosurgery is bloodless treatment, a very low incidence of infection, and a relative lack of scarring and pain.<sup>6</sup>

Various methods have been devised in the use of cryotherapy of lesions. They include the spray freeze technique, the applicator technique, the cryoprobe method, and the thermos-coupler method.

In open spray, the technique emits a fine spray of a cryogen on the target area. There is no contact between the tissue and the cryo gun tips, hence it will be preventing the instruments from sticking to the tissue, so it is useful for large, widespread, irregular, and multiple lesions and for those with a bleeding surface.<sup>7</sup>

Liquid nitrogen is the best and universal freezing source because of its low boiling point.

Several mechanisms are involved in cryotherapy for tissue damage.

1. By induction of tissue ischemia which causes damage to the blood vessels and capillaries within the target area which in turn leads to ischemic necrosis of the tissue.
2. By forming ice crystals and inducing osmotic cell injury and cellular membrane disruption.

In recent times, it has been determined that most tissue freeze at  $-2.2^{\circ}\text{C}$  and that temperature must fall below  $-20^{\circ}\text{C}$  for cell death to occur. According to dermatological guidelines temperatures of  $-30^{\circ}\text{C}$  for small malignant lesions and aggressive repetitive freeze cycles at temperatures of at least  $-50^{\circ}\text{C}$  or more for tissue necrosis to occur. Accumulation of damage occurs as the lesion undergoes repetitive freeze and thaw cycles, immediately from the original tissue. However, latent damage is produced which progresses to severe damage and subsequent necrosis to tissue in the following days.

During the freeze cycle as the temperature drops, it is believed that extracellular water undergoes crystallization. Membrane lipids harden at low temperatures decreasing cell resistance to shrinkage. As extracellular stores of water diminish, the electrolyte concentration increases. To counteract this concentration gradient, intracellular water moves out of the cell, and this water becomes involved in the crystallization process. Also, intracellular ice formed remains trapped within the cellular membrane. As a result of these processes, intracellular electrolytes reach toxic levels, which becomes lethal to the cell. During a thaw cycle, cells at the periphery of the cryo lesion will take up and enter the cell which can lead to swelling and lysis. Further re-crystallization may contribute

to cellular damage, however, this phenomenon may be avoided if cells are thawed rapidly.<sup>4</sup>

By tangentially excising the exophytic component of the lesion, the proliferative elements within the submucous layer may be more directly exposed to cryosurgery, accounting for the high success rates in treating verrucous lesions.<sup>6</sup>

An additional advantage of the method is the ability to obtain histologic confirmation of the diagnosis. The primary advantages of the present technique are their ease of use, very low morbidity, limited postoperative care, no sophisticated equipment required, and most of all satisfactory results. The advantage of the present technique is easy to use, has very low morbidity, limited postoperative care, no sophisticated equipment required, and most of all a satisfactory result.<sup>6</sup>

### ***Mechanism of Action of Cryosurgery***

The basic technique of cryotherapy stresses rapid cooling, slow thawing, and repetition of the freezing process to maximize tissue destruction. The two methods recognized are a closed system with the use of probes and nitrous oxide, or an open system with the use of a liquid nitrogen spray or a cotton tip.<sup>4,12</sup> In the present case, a closed system was used. These probes follow the principles of Joule-Thompson expansion which enable substances to undergo a drop in temperature when moved from a high-pressure area to a lower-pressure area.<sup>4,11,12</sup> For instance, when nitrous oxide is released from the high pressure inside the cryoprobe to the lower pressure cryo tip, the drop in temperature allows freezing of the tissues to occur. At present, the optimal temperature of cell death is unclear, however, it has been determined that most tissues freeze at  $-2.2^{\circ}\text{C}$  and that the temperature must fall below  $-20^{\circ}\text{C}$  for cell death to occur.<sup>4,11,12</sup> Immediately following treatment, cryo-lesions are indistinguishable from the original tissue. However, latent damage is produced which progresses to severe damage and subsequent necrosis to the tissues in the following days.<sup>11,12</sup> During the freeze cycle as the temperature drops, it is believed that extracellular water undergoes crystallization. In addition, membrane lipids harden at low temperatures decreasing cell resistance to shrinkage. As extracellular stores of water diminish, the electrolyte concentration increases. To counteract this concentration gradient, intracellular water moves out of the cell, and this water becomes involved in the crystallization process. Also, intracellular ice formed remains trapped within the cellular membrane. As a result of these processes, intracellular electrolytes reach toxic levels, which become lethal to the cell. During a slow thaw cycle, cells at the periphery of the cryo-lesion will take up excess electrolytes. To equalize this gradient, water enters the cell and can lead to swelling and lysis.<sup>12</sup> Cryotherapy is well-received by patients due to a relative lack of discomfort, the absence of bleeding, and minimal to no scarring. It is an effective, simple, predictable, relatively self-limiting, and safe method for almost all types of oral lesions. As it causes necrosis and sloughing as part of treatment, delayed healing is an inherent problem with this technique else, it is free from complications such as pain, hemorrhage, infection, inadvertent damage to adjacent structures, or scar formation that is seen with knife excision or electrosurgery. Surgical excision and sutures can make children and parents anxious. Cryotherapy can be repeated without permanent side effects and is more localized in action than radiotherapy or chemotherapy. Perhaps its greatest

advantage is its usefulness in candidates for whom surgery is contraindicated due to either age or medical history.<sup>12</sup> The main disadvantage of this technique is the lack of a specimen to be examined microscopically to confirm the diagnosis. Other disadvantages include an unpredictable degree of swelling and lack of precision with depth and area of freezing.<sup>12</sup> According to Farah and Savage, current protocols suggest that for most benign mucosal lesions, a 1 to 2 min freeze-thaw cycle using a cryoprobe is sufficient.<sup>4</sup>

## CONCLUSION

This case report used cryotherapy for the treatment of oral precancer. Cryotherapy seems suitable for treating thin or relatively thick plaque type precancerous lesions such as verrucous hyperplasia. Cryotherapy is one conservative management for the treatment of benign and malignant lesions. By careful selection of patients, cryotherapy is a simple, safe, easy, conservative, and acceptable treatment modality for certain types of benign oral lesions and oral precancers.

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