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Case Report

Management of Human Papillomavirus Associated Oral Lesions with Topical Acyclovir: Two Case Report

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Abstract

The purpose of this paper is to present the findings on the effective topical treatment of HPV-associated lesions using topical Zovirax. Two patients presented with HPV related lesions discovered on routine examination. The findings indicate that this topical antiviral treatment is effective, non-invasive, and cost-efficient, while also posing a lower risk over a reasonable duration compared to other therapeutic options. There has been only one prior report documenting the use of 1% cidofovir gel on gingival lesions in an HIV-positive individual, and the first report concerning Heck's disease. This approach is of significance especially in immunocompromised or those with polypharmacy.

Key Words: focal epithelial hyperplasia; heck disease; Zovirax; human papilloma virus; topical

Introduction

Human papilloma virus (HPV) is a DNA virus with more than 200 related viruses.[1] It can infect skin and mucous membrane by skin-to-skin contact, oral-genital contact, and oral-oral contact and induce benign or malignant tumor formation. Benign oral lesions are associated with low-risk HPV types 2, 4, 6, 7, 11, 13, and 32, with low potential for evolving to malignancy while malignant oral lesions are associated with high-risk HPV types 16, 18, 31, 33, 35, 39, 42, 45, 51, 52,56, 58, 59 and 66. [2] The benign HPV-related lesions found in the oral cavity include verruca vulgaris (common wart), squamous papilloma, condyloma acuminatum, and multifocal epithelial hyperplasia. In contrast, malignant HPV infections can result in dysplasia, verrucous carcinoma, and squamous cell carcinoma. Clinically, lesions associated with oral HPV are frequently asymptomatic, characterized by a soft, exophytic appearance resembling cauliflower, and may be pedunculated. Although the majority of HPV infections are asymptomatic and tend to resolve spontaneously, a biopsy is essential for diagnosing persistent infections, particularly those involving high-risk HPV types such as HPV16, which have the potential to undergo malignant transformation.[2,3]

Treatment of HPV infections depends on the area involved and the extent of the lesions but the treatments available cryotherapy, electrosurgery, surgical excision, laser, and trichloroacetic acid (TCA).[4,5] Surgical approach has been the most used therapy; however, it is difficult in more extensive lesion such as that in focal epithelial hyperplasia. Pharmacological treatment such as antiviral and immune therapy are rare but has been reported to be effective especially in recurrency. Acyclovir is an antiviral used for lesions of viral infections. It is administered via oral, intravenous, topical, or intralesional routes. It is approved by the FDA for the treatment of genital, skin, or oral herps lesions. [6,7] However, it is not commonly used as a stand-alone topical treatment for HPV related oral lesions, as few to none were reported in literature. We report two cases of HPV related oral lesions treated by topical acyclovir.

Case 1:

A 54-year-old male presented with complaints of "toothache." Upon examination, a single round papule measuring 5x5 mm was observed, characterized as a sessile exophytic white lesion with a cauliflower-like appearance, located above the interproximal area between teeth #13 and #14.

The lesion was keratotic, not ulcerated or inflamed. Medical history indicated that the patient underwent a kidney transplant in 2005, radical prostatectomy in 2022 and recent surgery removal of papillomatous pedunculated papule on the left marionette fold skin tags on the medial thigh. On Cyclosporine 100 mg q12hours, Mycophenolate mofetil 1g bid, Prednisolone 5 mg, Metformin 500 mg TID, Irbesartan 150mg, Atenolol 25 mg, Simvastatin 20 mg and Aspirin 81 mg. A diagnosis of an HPV-related lesion was considered; however, a biopsy was not performed due to the patient's condition. Zovirax 5% W/W Cream TID for 2 weeks, apply with a cotton swab and completely cover the area. Follow-up visits was planned along with comprehensive dental treatment.

Figure 1: Clinical picture of case one (A) before therapy, (B) after therapy.

Case 2:

A 29- years old female presented with painless soft multiple sessile papules on oral mucosa discovered on routine examination by her dentists. Lesions were not ulcerated or inflamed. She had no significant medical history and was not taking any medications. The intraoral examination showed papules that ranged from normal to white in color, primarily located on the buccal mucosa, and the lower lip mucosa. The clinical diagnosis of focal epithelial hyperplasia to confirm the diagnosis punch biopsy was performed on buccal mucosa. Histopathological assessment showed a squamous epithelium parakeratosis, koilocytosis of numerous epithelial cells, epithelial hyperplasia with evidence of viral cytopathic changes but no epithelial dysplasia was observed. Zovirax Suspension 200 Mg/ 5ml BID for 2 weeks, rinse, keep for 10 min then spit. Patient was seen in follow-up visits for 3 weeks (Figure 2& 3)

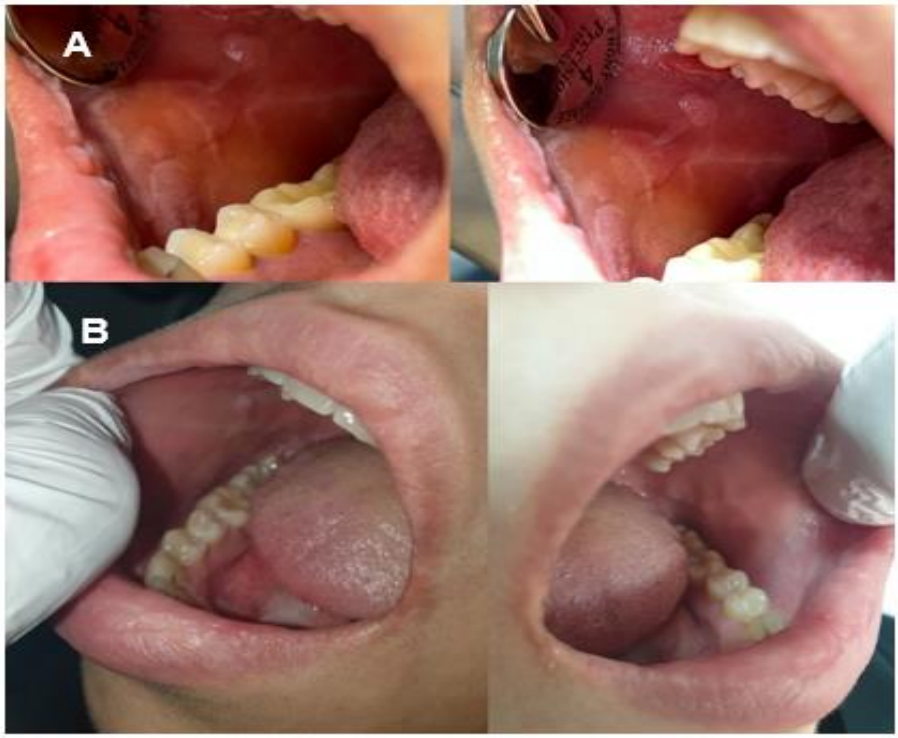

Figure 2: Clinical picture of case two (A) before therapy, (B) after therapy.

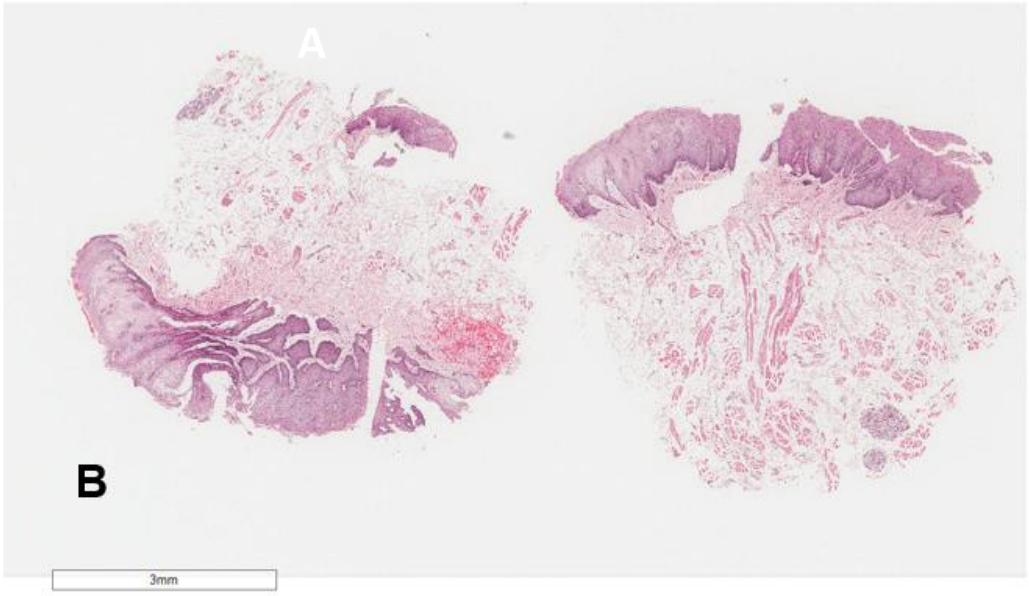

Figure 3: H& E section of second case showing a squamous epithelium parakeratosis, koilocytosis of numerous epithelial cells, epithelial hyperplasia.

Discussion

The most predominant HPV subgroup is the alpha group, which primarily targets mucosal epithelia with its HPV genotypes. This is followed by the beta group, which prefers infecting cutaneous epithelia. HPV initiates a productive lifecycle by infecting basal epithelial stem cells. Access to the cells is enhanced by micro-abrasion, trauma, or by regional characteristics such as tonsils.8 Intraorally, it can manifest in various forms, such as squamous papilloma, multifocal epithelial hyperplasia, verruca vulgaris and condyloma acuminatum. [3,8]

Management typically adopts a conservative approach, which may involve excision, CO2 laser treatment, electrosurgery, or cryotherapy. In cases of larger lesions, more extensive surgical interventions may be necessary. Although topical pharmacological therapies have demonstrated success in treating skin lesions, their efficacy in the oral cavity remains inadequately researched.[8,9] Various therapies available for cutaneous lesions include salicylic acid, lactic acid, retinoic acid, cantharidin, bleomycin, 5-fluorouracil, interferon alfa, podophyllotoxin, imiquimod, cidofovir and Vaccination. [10–12] In one of the reported cases chewing custard apple leaves was effective in HPV lesion therapy.[13] Acyclovir cream has been shown to be effective against Herpes Simplex with minimal side effects.[14] Acyclovir was initially described by Schaeffer and colleagues as a highly selective inhibitor of the replication of herpes viruses, achieved by inhibiting the synthesis of viral DNA. This inhibitory action relies on its interactions with thymidine kinase and DNA polymerase. Acyclovir is offered in various forms, including intravenous, oral, and topical applications. The topical formulation of acyclovir is available as 5% cream and ointment. [6,7] Numerous studies have shown the effectiveness of topical therapies, achieving high remission rates; however, the complete elimination of the HPV virus continues to be an unattainable goal.[12]

The application of topical therapy could be advantageous for patients with medical vulnerabilities, older adults, and individuals who are not candidates for surgical interventions, laser treatments, or alternative therapies. Furthermore, it contributes to the reduction of lesions, particularly in cases of focal epithelial hyperplasia (Heck's disease). It may also prove beneficial in terms of cost efficiency, minimizing side effects, and facilitating the scheduling of appointments. To date, only one previous case report has employed 1% topical cidofovir gel in a patient diagnosed with HIV, and it was found to be effective. [15,16]

Conclusion

In summary, topical antivirals are generally well tolerated and have demonstrated satisfactory outcomes. This treatment approach may be particularly beneficial for patients with specific constraints. We recommend further investigations to confirm the results using a larger number of participants.

Conflict of interest declaration: The authors report no conflicts of interest in this work.

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