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Case report

Post-Operative Intraoral Herpes Infection of the Hard palate – An appraisal and Case Report

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Abstract
Herpes simplex's virus-1 (HSV-1) commonly infects the mucosal layer of different human organs. This case reports a 60-year-old man suffering from the HSV-1 infection of the hard palate after a dental procedure. Personal history, a thorough medical examination, and laboratory tests confirmed a recurrent infection by HSV-1. Many pre-disposing factors may reactivate HSV-1 virus from its' latent phase. Prescribed therapy was to relieve symptoms and to optimally accelerate healing time. No vaccine exists against HSV-1but recrudescence of the infection may be prevented with targeted management and prophylactic measures.

Keywords: Complication, post-operative, Herpes simplex, injection, intra-oral, palate, therapy, ulcer

Introduction
Herpesviridae are constituted by numerous structurally complex viruses that contain double stranded DNA genomes. There are eight known types of human Herpes Viruses: Herpes simplex types 1 and 2 (HSV-1 and HSV-2); Varicella zoster (VZV, HSV-3); Epstein-Barr Virus (EBV HSV4); Human cytomegalovirus HCVM, HSV 5); Human herpes virus 6(HSV-6); Human herpes virus 7 (HSV-7); and Human herpes virus 8 (HSV-8). These eight are grouped into three subfamilies: the alpha-herpes viruses that embraces HSV-1, HSV-2 and VZV. These have rapid reproduction cycles and invade sensory - and establish themselves as latent viruses – in sensory ganglia. The beta- and gamma-herpesviruses are lymphotropic. These two groups are distinguished from each other and the Alpha group on the basis of their genomes-organization and patterns of replication [1]. The Herpes simplex viruses 1 and 2 that are ubiquitous, host-adopt- ed, and both cause similar lesions, but are different diseases. These initial two types are named HSV-1 and HSV-2, but also labeled as Human alpha herpes virus 1 and Human alpha herpes virus 2 [1]. Historically the virus was known with mention of lip lesions going back to early classical Greek civilization about 2500 years ago. Traditionally the HSV-1 virus is associated with orofacial diseases, specifically on the mucosal layers, whereas Herpes-2 affected the genitalia [2]. This report is targeted at all healthcare workers, but specifically oro-dental health-care workers.

Aim
This case presentation reports clinical findings of palatal Herpetic ulcers after a local analgesic injection for a dental restorative procedure, appraises Herpes pathogenesis and discusses treatment modalities for the palatal post-operative Herpes lesion.

Herpes simplex virus type 1 is an enveloped virus with an icosahedral capsid with a diameter of 100->110 nm containing double stranded DNA. The virus belongs to the Alpha-herpesviridae subfamily, and the HSV-1 follows a complex pathogenic cycle. HSV-1 causes an initial infection of epithelial cells, as a primary gingivo-stomatitis, and then latency in the supplying neuron and finally undergoes the reactivation phase. It is responsible for the primary and the recurrent vesicular blister infections in the oral mucosae and skin. Most HSV-2 infections are genital, as HSV-I may impart partial immunity to HSV-2. The prevalence of oral HSV-2 infections may be higher than clinically diagnosed because unlike HSV-1, HSV-2 infection rarely reactivates and accordingly goes undetected. HSV-1 can be spread by both oral routes and genital sex [3,4]. HSV-1 and HSV-2 infection may manifest with a wide variety of exhibiting stigmata, including orolabial herpes, herpetic whitlow, psychoses, herpes meningitis, pan-encephalitis, herpes gladiatorum, lesions on the skin, vulva, uterus, or penis, and eczema herpeticum [5-7].

Case Presentation
A 60-year-old man presented for a dental examination: his main complaint was pain from his upper right molars. He suffered from low-level pain while brushing or flossing those teeth. He revealed a history of tobacco-smoking (10 cigarettes, half pack a day) for 40 years. He had an aortic valve replacement by a mechanical valve due to narrowing of his aortic valve and a concurrent history of rheumatic heart disease 28 years previously. He was medicated with 5mg Warfarin daily and 10000 international unit of vitamin D once a week. His prothrombin time test and international normalized ratio (PT/INR) was controlled from exceeding acceptable thresholds (at 2.5), and he complied fully with instructions from a hematologist. He reported no medicinal hypersensitivity or allergy to any medication.rence of HSV-1 indicates a second or third episode of the viral infection with pre-existing but inadequate antibodies to that virus [11].

A thorough oro-dental examination, including a 'bitewing' and intra-oral 'periapical' Radiographs, revealed the patient had a recurrent carious lesion on tooth #16 distal surface (Figures 1-2). No periapical lesion or radiolucency was present. A direct composite restoration was prescribed, and also a prophylactic antibiotic cover with 2g oral amoxicillin 1 hour before presentation. Topical analgesia was achieved with 20% benzocaine surface gel, followed by a buccal infiltration injection of 1.7mL of 4% Articaine with 1:200 000 epinephrine. Upper molars usually have three roots, two buccal and one palatal. To ensure adequate analgesia of the palatal root and the palatal marginal gingiva, a right unilateral greater palatine nerve block was administered. The defective restoration and decay were successfully removed and replaced with a #16DO composite resin-restoration, with a resin-modified calcium silicate liner.

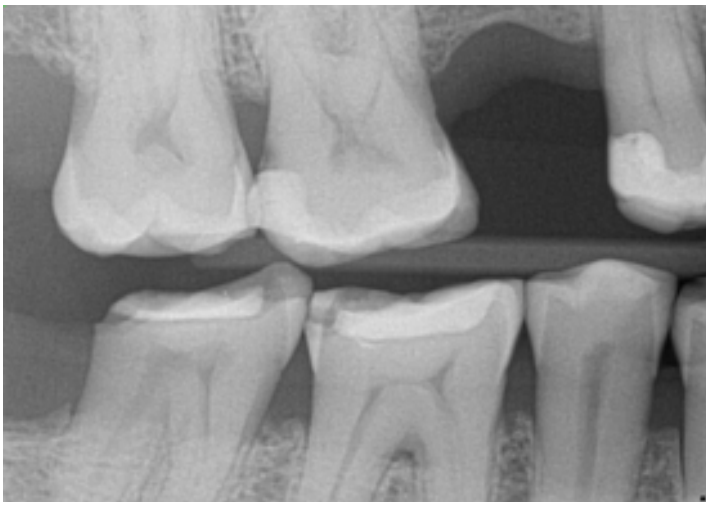

Figure 1: Pre-Operative intra-oral 'bitewing' film of the right side. Tooth #16 is included.

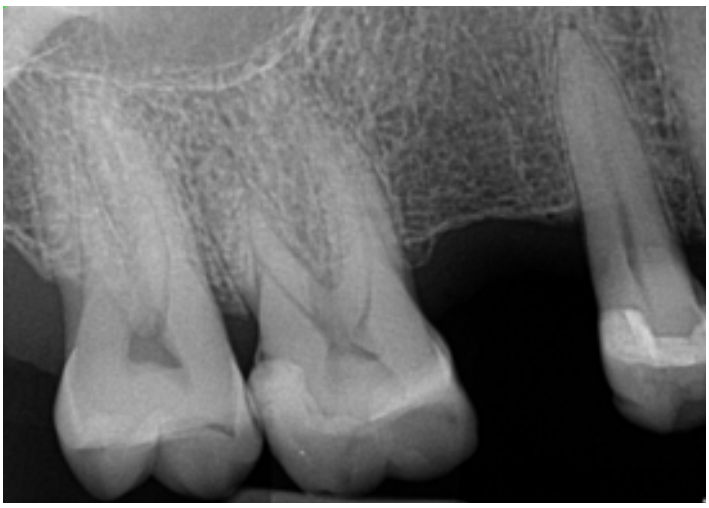

Figure 2: Pre-Operative intra-oral 'periapical' film of the tooth #16.

After one week the patient returned complaining of pain from the same tooth. Vitality-testing indicated the tooth #16 was vital; the tooth seemed healthy, and a simple occlusal adjustment ruled out any occlusal trauma. At that appointment, the whole palatal mucosa appeared healthy. But some palatal pain persisted, and after 10 days from the visit, to replace the restoration, he presented with multiple small circular ulcerated lesions on the palatal keratinised mucosa adjacent to tooth #16 (see Figure 3). He reported a sore throat, mild headache and a pain radiating to the right temporal region. He had no fever, dysphagia or loss of appetite, but he complained of a sharp and intense pain when eating or touching the affected area. A provisional differential diagnosis included recurrent herpes simplex, herpangina or herpes zoster.

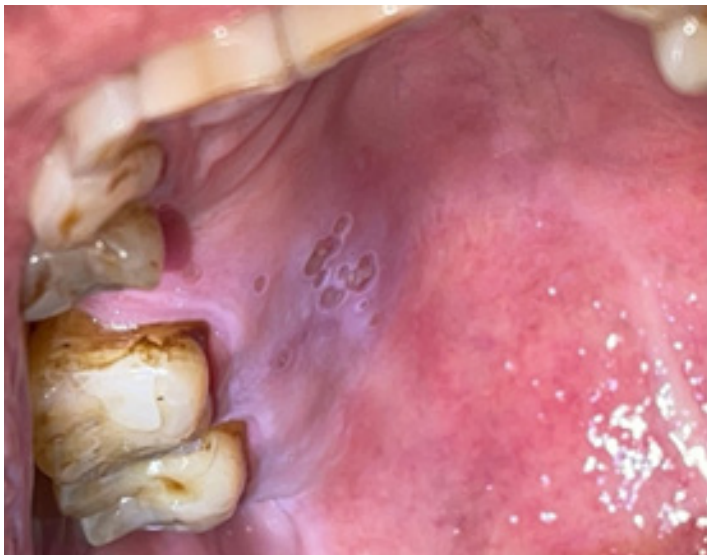

Figure 3: Multiple small circular ulcers on the hard palate (arrow) observed at presentation.

For special investigations, a bacterial specimen for culture identification was ordered and a swab for a Tzanck smear (cytological exam). For treatment Acyclovir 400 mg three times daily for 10 days was prescribed and a mouthwash solution of lidocaine 2% for pain relief. The following day the patient was seen again (see figure 4) and subsequently two-day follow-ups visits monitored progress of the lesion. The individual ulcers (1mm diameter) fused together to form one, larger 5mm amorphous crenulated ulcer, which slowly shrunk in diameter, and after nine days eventually disappeared (see figures 4 to 7).

The lesions developed on the mucosa overlying the right greater palatine nerve, over the site of needle puncture during the local analgesia block. This micro-trauma may have been the trigger for viral activation.

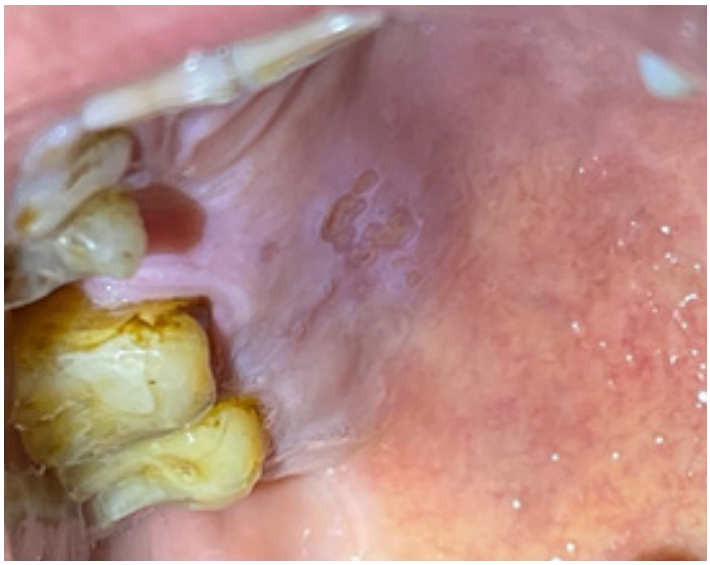

Figure 4: Coalescing of the ulcers at day 2 (Acyclovir was already prescribed).

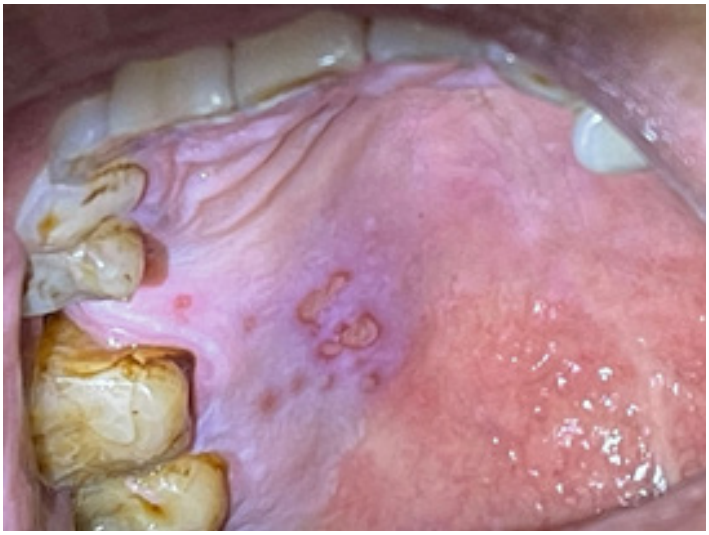

Figure 5: Ulcers healing covered with debris and exudate. Note: the palatal mucosal surface keratinization appears opaque as the patient was avoiding.

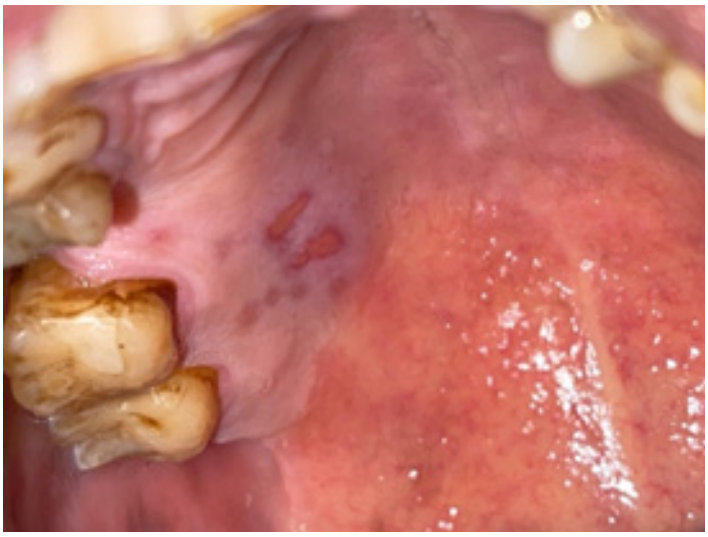

Figure 6: Healing ulcers reduced in size. The palatal mucosal color is returning to stable health.

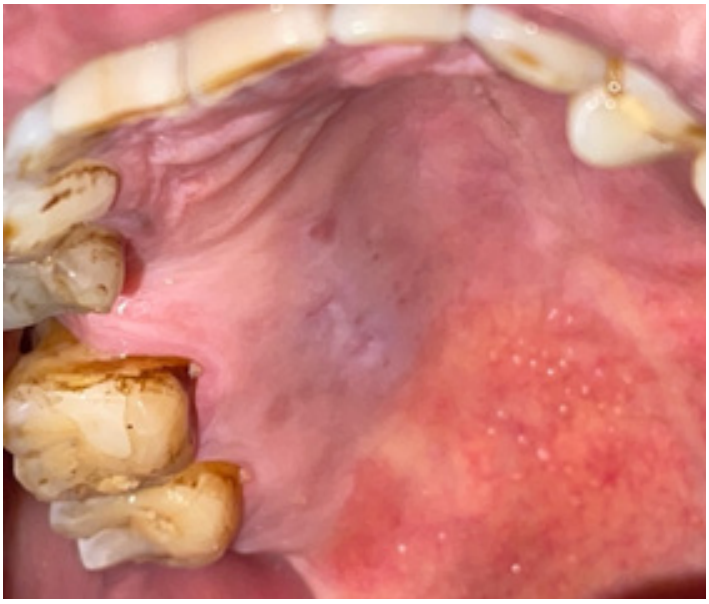

Figure 7: Healed palate after 9 days residual scar area still visible. Note: Peri-cervical staining from tobacco smoking.

Results

The bacterial-culture growth revealed a preponderance of Staphylococcus Capitis bacterial colonies. This bacterium is acknowledged as among the major putative pathogens involved in the formation of prosthetic valve endocarditis [8,9]. This highlights the importance to evaluation a patient's previous history. Besides Staphylococcus capitis, other colonies of Staphylococcus hyicus, Micrococcus luteus, Candida yeast and Bacillus licheniformis were observed. There was no mention of Streptococcus spp, like S. viridans in this particular case. Histological examination of such a lesion typically shows ballooning degeneration of infected epithelial cells, inclusion bodies, fusion of cells to form syncytia of multinucleated giant epithelial cells, and the formation of Tzanck cells with acantholysis, all of which are pathognomonic of Herpes viral infections. See figure 8, which is not derived from the case reported here.

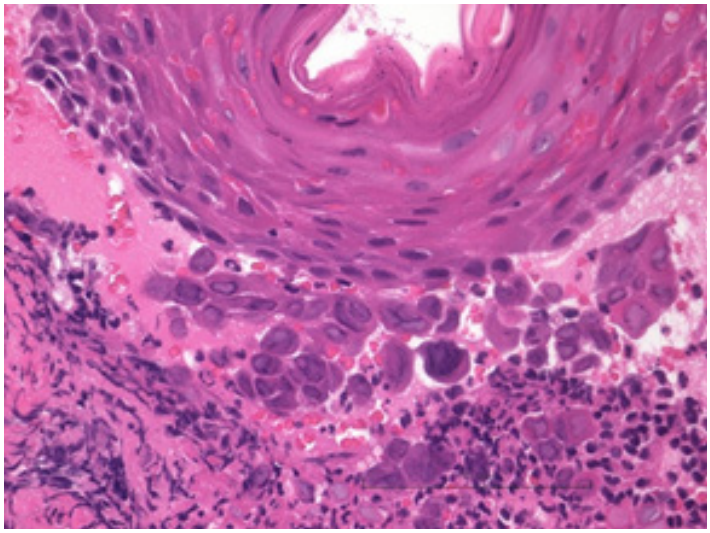

Figure 8: Microscopic H&E stain examination of a biopsy with multilobular nuclei and cell abnormalities pathognomonic of Herpes viral infections. Note: this histopathological slide specimen was not from the patient described here.

Discussion

HSV-1 and HSV-2 are causally related for recurrent facial and genital herpetic lesions, and although they are painful, they are generally not life threatening. Herpes labials, nasalis and ophtalmicus, may occur. A Herpes infection that disseminates to the brain is potentially lethal as an infection in an immuno-compromised person or newborn. HSV-1 infection of the eye may lead to blindness. This patient was a smoker and was possibly slightly immuno-compromised but showed no signs that his brain or eye-sightwas affected. Each type of Herpes virus will cause a specific disease. These diseases are more prevalent and have become manifest in immuno-compromised people. HSV-1 causes labial cold sores, HSV-2 causes genital lesions, HSV-3 causes Shingles (Varicella-Zoster), HSV-4 causes Glandular Fever, Burkitts' lymphoma and naso-pharyngeal carcinoma, HSV-5 is associated with congenital abnormalities, HSV-6 causes infant exanthema subitum rashes, HSV-7 causes febrile illness and HSV-8 causes Kaposis sarcoma. The physical examination of this patients' results from the swab tests and the patient history confirmed the clinical diagnosis of recurrent HSV-1 infection of the hard palate. Most of the initial HSV-1cases take place in the oropharyngeal mucosa as primary Herpetic gingivo-stomatitis, or recurrent Herpes labialis. [10, 11]. HSV-1 often settles in the Gasserian ganglion and has been implicated in other cranial nerve syndromes like: - Facial VII Nerve (Bells' palsy), Auditory VIII Ramsay-Hunt syndrome, Vagus X and IX Glossopharyngeal pathologies. HSV-2 can affect the pudendal and inguinal sensory ganglia. Experimentally it has been observed that the trigeminal ganglion is colonized and harbors the latent virus [10]. The primary infection develops in a susceptible host (host without pre-existing effective antibodies of HSV-1). Recur

The concept of recurrent infection is interlinked with the viral latency. The molecular latency begins with entry of the of HSV-1 infecting the nerve endings and spread of the virus to the nuclei of the sensory ganglion in place through centripetal spread. Multiplication of the virus takes place in the sensory neurons leading to the cells' eventual destruction. In the majority of the infected neurons, the viral genome persists in a dormant state for life. In some cases, the virus is reactivated and transported back to the site of portal entry through centrifugal neuron axonal transport [10,11].

HSV-1 and HSV-2 may interchange and can only be differentiated and determined with serology. Exact reasons for the reactivation of the virus, including the systemic, or the local stimuli, remains obscure. But the reactivation of the virus seems to depend upon some stimulus of the peripheral nerve pathway and anterior nerve route. Recurrence may even take place with proven established humoral- and cell-mediated immunity. Most recurrences are unpredictable and/or spontaneous, yet there is always some association with emotional or physical stress, tissue damage, fever, exposure to the ultraviolet light, and/or immune suppression [12,13]. Besides concern over the effectiveness of the antiviral treatment, there are some recommendations for treatment and management of the oro-labial and palatine herpes. Valacyclovir, famciclovir and acyclovir through oral route are recommended until the disappearance of the infection. As supportive oral therapy, topical application of local analgesic paste markedly relieves pain [15]. Below is a table-list of antiviral drugs available as supportive therapy, all of which will help moderate active Herpes proliferation.

Antiviral therapies

Following is the list of available antiviral medications.

Table 1: List of antiviral medications [16,17].

Medication	Dose rate	Route
For first outbreak of oral herpes		
Acyclovir	400mg three times a day for 10 days	Orally
Valacyclovir	2000 mg every twelve hours for one day	Orally
Famciclovir	250 mg three times a day for 7 to 10 days	Orally
For Recurrent infection		
Acyclovir Cream 5% for recurrent herpes labialis (Zovirax)	5 g apply 4-6 times daily for 7-10 days	Topical
Acyclovir	• 400 mg three times a day for 5 days • 800 mg twice a day for 5 days • 800 mg three times a day for only two days	Orally
Valacyclovir	2000 every twelve hours for one day	Orally
Famciclovir	1500 mg once a day	Orally

There is no ideal protocol for management of cases like this [11]. Stress seems to alter a persons' metabolic state with reduced immunity, and this predisposes them to possible infections and to recrudescence of latent Herpes infections. Accordingly, implementation of stress reduction strategies including adequate rest and sleep, would assist in moderating the occurrence of Herpes infections [13]. For effective prevention of secondary infection, sustained oral hygiene is recommended. This involves regular tooth brushing, flossing of inter-dental spaces, aided by frequent oral lavage with saline or some other antiseptic mouth wash. It is desirable to avoid physical contact with someone who has an active herpes infection. The use of facial cosmetics such as lip-balms, lotions, lipstick, creams and oral-hygiene paraphernalia like tooth-brushes, mouth-rinses, and floss-holders, should never be shared, and should be strictly retained for one-persons' individual personal use. During the outbreak phase, hand washing with anti-septic soap or frequently sanitizing the hand with 60% ethanol solution would strongly assist in reducing viral spread and reduce any cross contamination of viruses to others, or to other parts of the body. Use of gloved hands (single-use), impervious transparent facial-screens and strict antiseptic techniques are mandatory for dental health care workers treating Herpes-infected patients. After applying topical treatments to any infected region, gloved hands should be washed immediately, and the used gloves disposed of [18].

Concluding remarks

There is no accepted optimal protocol, or any effective vaccine available, to treat this type of palatine HSV-1 infection [15]. Antiviral and supportive therapies are recommended for symptomatic relieve and to avoid secondary infection. Medication should always be according to the severity level. In typical cases the local lesions heal within two weeks, but the healing time and pain can be noticeably shortened with the help of available anti-viral medicines and topical analgesic pastes. Most importantly for prophylaxis is the reduction of predisposing stress factors and avoiding direct physical contact to stop viral spread.

Conclusion

Post-operative Herpes infection after dental procedures is well known, but rare. Most cases heal within a fortnight, but treatment with antivirals and topical analgesic paste hastens healing, relieves pain, and discomfort and prevents secondary infection.

Author statement

The authors have no conflict of interest to declare. Patient informed consent was secured. No IRB certificate was needed for this report.

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