Severe herpes simplex virus type-I infections after dental procedures

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Abstract
Background: Recurrences of herpes labialis (RHL) may be triggered by systemic factors, including stress, menses, and fever. Local stimuli, such as lip injury or sunlight exposure are also associated to RHL. Dental extraction has also been reported as triggering event.

Case reports: Seven otherwise healthy patients are presented with severe and extensive RHL occurring about 2-3 days after dental extraction under local anaesthesia. Immunohistochemistry on smears and immunofluorescence on cell culture identified herpes simplex virus type I (HSV-I). Five patients reported more severe prodromal signs than usual. Although all the patients suffered from RHL, none had previously experienced RHL after dental care. Two patients required hospitalisation for intravenous acyclovir therapy, whereas the others were successfully treated with oral valaciclovir or acyclovir.

Conclusion: Severe and extensive RHL can occur soon after dental extraction under local anaesthesia. Patients with a previous history of RHL seem to be at higher risk. It is not clear whether RHL is linked to the procedure itself, to the anaesthetic procedure or both. As the incidence is unknown, more studies are required to recommend prophylactic antiviral treatment in RHL patients who are undergoing extractions. Dentists should be aware of this potentially severe post-extraction complication.

Key words: Aciclovir, prevention, herpes labialis, triggering factors.

Introduction
Herpes simplex viruses type I (HSV-I) and II (HSV-II) are members of the α-herpesvirus family (1). The primary infection establishes a life-long latency in the sensory nerve ganglia. Subsequent infra-clinical recurrences are common, eventually followed by a clinical recrudescence (1). Recurrent herpes labialis (RHL) affects 16% to 38% of the population (1). In elderly patients, the frequency of RHL sinks to approximately 20%. The recrudescence of HSV infections requires simultaneously viral reactivation at the trigeminal ganglia level as well as a cutaneous permissivity allowing intra-epidermal viral replication that lead to lesion formation (1). Recrudescence is usually occurring at the same anatomical site, in general the vermilion border of the upper or lower lip. Recrudescences often present a similar clinical course in terms of duration, pain and lesion severity (1). In many instances, RHL follows
various initiating events. Systemic stimuli include fever, menses, iatrogenic immunosuppression and stress. Local triggers encompass lip injury, exposure to cold, sunlight, wind, and iatrogenic trauma (1). RHL can also complicate dental procedures, fixed prosthodontic tissue, and surgery of the oral cavity (1-6). Although supposed to be rare, no data on the incidence of dental intervention-associated RHL are available.

Seven patients are described who presented unusual extensive and severe HSV-I infection following dental extraction.

Case Reports
The salient clinical features of the patients are summarized in Table 1. None of the patients presented a remarkable medical, allergic or surgical previous history. The patients took no immunosuppressive medication. All the patients (3 males/4 females, mean age: 37.2 years, minimum: 19 years, maximum: 55 years) suffered from long-standing RHL, experiencing between 3 and 8 recurrences per year. Stress was the most frequent initiating event. Two patients suffered from sun-exposure related recurrences. Previously, none had experienced RHL after dental care. Five patients systematically recognized the typical prodromal signs, including stinging, burning, dysesthesia, and itching, occurring 1 to 2 days before the recurrences. Preceding the current episode, the prodromal signs were much more severe than usual.

The patients searched medical advice mainly due to the unusual severity of the eruption. Five patients visited the emergency ward and the others consulted their GP or dermatologist. One of the patients admitted to the emergency ward was initially misdiagnosed as erysipelas and received intravenous antibiotics (Amoxicillin/clavulanic acid, Augmentin®, 3x1000mg/day, Smith Kline Beecham). Two patients presented a painful eruption extending to the right cheek, nose, chin, the oral cavity and upper lip (Fig 1, 2). Erythematous, vesicular, and crusted lesions were present. Both had fever (39°C), a regional adenopathy and were not able to eat. Further physical examination was unremarkable. Due to the severity, two patients required hospitalization and intravenous acyclovir (5mg/kg/day for 8 days, Zovirax®, Glaxo Smith Kline) was administered 48 hours before until three days after dental care. No further herpetic recurrences were observed in both patients. The drug was well tolerated.

Tzanck smears were performed in 6 patients showing multinucleated, syncytial giant cells and numerous polymorphonuclear neutrophils, suggesting an α-herpesvirus infection. Immunohistochemistry using specific antibodies directed against HSV-I, HSV-II and Varicella Zoster Virus (VZV) (7) revealed a positive signal for HSV-I, whereas the other antibodies revealed a negative staining. In one patient, a swab was performed for viral cell culture, revealing HSV-I by immunofluorescence after 48 hours. The alveolar healing process after extraction was not impaired or delayed.

Two patients required subsequent molar extractions and prophylactic oral valaciclovir (500mg b.i.d., Zelitrex®, Glaxo Smith Kline) was administered 48 hours before until three days after dental care. No further herpetic recurrences were observed in both patients. The drug was well tolerated.

In the five other patients the eruption extended beyond the usual site of recrudescence to the nasolabial fold, the chin, and the cheek, predominantly affecting the site where the procedure had taken place. The patients were treated with oral valaciclovir (Zelitrex®, 500mg b.i.d. for 7 days) or oral acyclovir (5 x 200 mg for 7 days). All the patients presented the recrudescence 2 to 3 days after the dental interventions. All the procedures (Table 1) were performed under local anaesthesia using lidocaine (either block anaesthesia of the inferior alveolar nerve or local periodontal infiltration for upper molars). The procedures were molar extractions (5), incisor extraction (1) and renewal of a filling (1).
Discussion

Seven cases of severe dental-extraction-related HSV infections are presented. The imputability to dental injury should be taken with precaution. Nevertheless, all the patients had a previous history of RHL, no history of RHL following dental fillings, no RHL at the time of extraction, a significantly more severe eruption than usual, local anaesthesia, a time-interval of 2-3 days, and an increased healing time of the eruption in common. All the recrudescences started at the site of prior episodes. Although dental extraction is usually incriminated as initiating factor, HSV may also complicate fixed prosthodontic tissue (4). There are no data concerning other common dental procedures, such as fillings or removal of dental plaque. Data on frequency of extraction-related RHL are sparse and contradictory. In a study, 4/20 patients with a previous history of RHL experienced RHL after dental extraction whereas no recurrences were noted in 19 patients without a history of RHL (2). However, in a large study evaluating the post-extraction complications of 3818 extractions, no single case of HSV was evidenced (8). In another study comprising 48 patients undergoing third molar extraction showed that the frequency of HSV-1 positive nested polymerase chain reaction (PCR) was low (4.2%) and not statistically significant with a control group undergoing conventional procedures (5).

The triggering may be multi-factorial. First, it has been demonstrated that fear and stress for dental procedures increases HSV asymptomatic shedding (9). This may be further increased by the nerve injury during extraction (9). In fact, during surgical procedures involving the trigeminal nerve root, HSV reactivation occurs in up to 50% of the patients (10). However, HSV shedding seems to occur independently from clinical recurrences (11,12). Third, nerve irritation by the anaesthetic block may also conduct to viral reactivation and recrudescence, as the inferior alveolar nerve is a branch of the mandibular nerve, which is itself the third branch of the trigeminal nerve, where viral latency is established. These three elements probably lead to a higher viral load, explaining the increased severity of the eruption. Extension of HSV cutaneous extension is often facilitated by keratinocytic injury, observed during deep chemical peelings, abrasive laser resurfacing, dermabrasion and other cosmetic procedures (13). However, no signs of prior skin injury were present in the patient. It is unclear, whether the manipulation and extension of the lips during the dental procedure constitutes a risk factor. The alveolar healing process after extraction seems not delayed or impaired.

The clinical diagnosis of extraction-related RHL is usu-
ally evident. However, immunohistochemical confirmation on a Tzanck smear is suggested (7), in particular as post-extraction herpes zoster has been described (14,15). As sero-prevalence achieves 90 to 95% in the adult population, serology is not a recommended diagnostic method.

The treatment of these extraction-related HSV infections relies on oral or intravenous antiviral therapy, according to the clinical severity. In two patients, prophylactic antiviral treatment was effective as no RHL was observed after subsequent molar extractions under local anaesthesia. More data is however required to recommend prophylactic antiviral therapy. Currently, only selected individuals with a history of RHL are eligible for antiviral prophylaxis. In analogy to prophylactic antiviral treatment for abrasive cosmetic procedures, the following scheme could be proposed; oral valaciclovir (500mg b.i.d., Zelitrex®, Glaxo Smith Kline), 48 hours before until three days after dental care. Famciclovir or acyclovir may also be considered (13).

In conclusion, recrudescence of HSV can be triggered by dental extraction. These infections seem to be more severe than usual outbreaks. Data on incidence are lacking. Prophylactic antiviral treatment could be considered for RHL patients on an individual basis. Dentists should be aware of this potentially severe complication of dental extraction.

References