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 permissiveness 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, erosive lesions were observed on the nasolabial fold, chin, lower lip, and earlobes. The skin was edematous, tender, and warm to the touch.

Fig. 1. Severe HSV-1 infection following extraction, affecting the lips, cheek, nose, and oral cavity.

Fig. 2. Severe and extensive HSV-1 infection after molar extraction.

Table 1. Salient patient characteristics.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Procedure</th>
<th>Anaesthesia</th>
<th>Time interval extraction-RHL</th>
<th>Signs</th>
<th>Site</th>
<th>Test</th>
<th>Serology</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>39</td>
<td>Extraction Sup R 3m</td>
<td>Local</td>
<td>2 d</td>
<td>Fe, Ad</td>
<td>Labial inf/sup Check, chin</td>
<td>Tz</td>
<td>IgG+, IgM-</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>19</td>
<td>Extraction Inf R incisor</td>
<td>Block</td>
<td>2 d</td>
<td>Fe, Ad</td>
<td>Labial inf/sup Check, chin</td>
<td>Tz</td>
<td>IgG+, IgM-</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>55</td>
<td>Extraction Inf R 2m</td>
<td>Block</td>
<td>2 d</td>
<td>-</td>
<td>Labial sup Chin Nasolabial</td>
<td>CC</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>21</td>
<td>Filling Sup R 1m</td>
<td>Local</td>
<td>3 d</td>
<td>-</td>
<td>Labial sup Chin Nasolabial</td>
<td>ND</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>30</td>
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<td>Block</td>
<td>3 d</td>
<td>-</td>
<td>Labial inf/sup</td>
<td>Tz</td>
<td>IgG+, IgM-</td>
</tr>
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<td>6</td>
<td>M</td>
<td>46</td>
<td>Extraction Inf R 3m</td>
<td>Block</td>
<td>2 d</td>
<td>-</td>
<td>Labial inf/sup</td>
<td>Tz</td>
<td>NA</td>
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<td>F</td>
<td>51</td>
<td>Extraction Inf R 2m</td>
<td>Block</td>
<td>3 d</td>
<td>-</td>
<td>Labial inf Chin, cheek</td>
<td>Tz</td>
<td>IgG+, IgM-</td>
</tr>
</tbody>
</table>

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®,
GSK). Both individuals had a positive past serostatus for
HSV (IgG: +, IgM: -). Topical and intraoral disinfection
with povidone iodine (Isobetadine®, MEDA Pharma)
was administered three times daily. Blood screening
only revealed a mild increase of the sedimentation rate.

Other laboratory examinations, including liver, renal,
and thyroid functions as well as red and white blood cell
counts were in normal range. Serology was negative for
HIV, hepatitis A and B.

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 lido-
caine (either block anaesthesia of the inferior alveolar
erve or local periodontal infiltration for upper molars).
The procedures were molar extractions (5), incisor ex-
traction (1) and renewal of a filling (1).

Tzanck smears were performed in 6 patients showing
multinucleated, syncytioid giant cells and numerous
polynuclear neutrophils, suggesting an α-herpesvirus
infection. Immunohistochemistry using specific anti-
body 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) administered 48 hours before
until three days after dental care. No further herpetic
recurrences were observed in both patients. The drug
g was well tolerated.

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 his-
tory of RHL following dental fillings, no RHL at the
time of extraction, a significantly more severe erup-
tion 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 com-
ipple 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 re-
currences 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 extrac-
tion showed that the frequency of HSV-I positive nested
polymerase chain reaction (PCR) was low (4,2%) and
not statistically significant with a control group under-
going conventional procedures (5).

The triggering may be multi-factorial. First, it has been
demonstrated that heat and stress for dental procedures
increases HSV asymptomatic shedding (9). This may be
further increased by the nerve injury during extrac-
tion (9). In fact, during surgical procedures involving
the trigeminal nerve root, HSV reactivation occurs in
up to 50 % of the patients (10). However, HSV shed-
ing seems to occur independently from clinical recur-
rences (11,12). Third, nerve irritation by the anaesthetic
block may also conduct to viral reactivation and recru-
descence, 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 facilitat-
ed by keratinocytic injury, observed during deep chem-
ical peeling, ablative laser resurfacing, dermabrasion
and other cosmetic procedures (13). These procedures
systematically require a prophylactic antiviral treatment
(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 confir-
mation on a Tzanck smear is suggested (7), in particu-
lar 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 diag-
nostic method.

The treatment of these extraction-related HSV infec-
tions relies on oral or intravenous antiviral therapy,
according to the clinical severity. In two patients, pro-
phylactic 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