CASE REPORT

# Burning mouth syndrome due to herpes simplex virus type 1

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## SUMMARY

Burning mouth syndrome is characterised by chronic orofacial burning pain. No dental or medical cause has been found. We present a case of burning mouth syndrome of 6 months duration in a healthy 65-year-old woman, which was associated with high copy numbers of herpes simplex virus type 1 (HSV-1) DNA in the saliva. Her pain resolved completely after antiviral treatment with a corresponding absence of salivary HSV-1 DNA 4 weeks and 6 months later.

## BACKGROUND

Burning mouth syndrome is a chronic, burning sensation in the mouth, with no underlying dental or medical cause. The burning sensation can be unilateral or bilateral and is localised to the lips, tongue, hard or soft palate. The prevalence varies from 0.7% to 7% and is seen in up to 18% of postmenopausal women.[1 2] Previous treatment has included antidepressants, cognitive behavioural therapy, analgesics, hormone replacement, α-lipoic acid and anticonvulsants.[3]

## CASE PRESENTATION

A previously healthy 65-year-old woman developed a burning sensation in her mouth, localised to the right buccal mucosa and anterolateral two-thirds of the tongue. The burning increased when she brushed her teeth and usually decreased within 10 min. Pain resolved spontaneously after 4 weeks. One year later, burning pain in the same distribution recurred and became constant. Dentists, including an oral surgeon, found no mucosal lesions or other abnormalities. No relief was provided by mouthwashes, milk of magnesia rinses, discontinuation of toothpaste with whitening agents or clonazepam. The pain continued for 6 months. The patient denied dysarthria, dysphagia, dry mouth, a history of cold sores or other medical problems. She did not abuse tobacco, alcohol or recreational drugs. On examination, an aphthous ulcer was seen on the right anterolateral tongue. Sensation was normal on the face, tongue and in the mouth. There was no loss of taste, tongue atrophy or weakness.

## INVESTIGATIONS

A complete blood count, liver, renal, autoimmune and thyroid function studies and brain MRI were normal. Saliva was collected and DNA extracted in a total volume of 100 µL as previously described.[4] Quantitative real-time PCR of salivary DNA (10 µL/reaction) using primers for cellular glyceraldehyde 3-phosphate dehydrogenase (GAPDH),[5] varicella zoster virus (VZV),[6] and HSV-1[6] and HSV-2[7] was performed as previously described.[6] PCR efficiencies for VZV, and of herpes simplex virus type 1 (HSV-1) and HSV-2 were similar (104, 104 and 102, respectively), and range of detection for all three viruses was 10–$10^6$ DNA copies per reaction. Saliva contained cellular GAPDH and $3.4\times10^8$ copies of HSV-1 DNA per mL, but no VZV or HSV-2 DNA.

## TREATMENT

The patient was treated with oral valacyclovir, 1 g three times a day for 10 days, followed by valacyclovir, 1 g daily for 1 year.

## OUTCOME AND FOLLOW-UP

The mouth pain resolved completely within 5 days after antiviral treatment. PCR of saliva 4 weeks and 6 months after starting antiviral treatment revealed no HSV-1, HSV-2 or VZV DNA. The patient has remained pain free for 1.5 years after discontinuing antiviral therapy.

## DISCUSSION

No prior reports have associated the burning mouth syndrome with HSV-1 or any other virus. HSV-1 is a ubiquitous human α-herpesvirus that becomes latent in most cranial nerve ganglia in up to 70% of individuals.[5] The trigeminal ganglion, which provides sensory afferent innervation to the face and mouth, is the most common cranial nerve ganglion infected.[8] HSV-1 reactivation typically causes recurrent cold sores (herpes labialis) and ocular disease (herpes keratitis). HSV-1 also causes facial pain and, rarely, encephalitis, and is associated with Bell's palsy,[9] all usually in the absence of rash. HSV-1 is shed in saliva of asymptomatic immunocompetent and immunocompromised individuals, although the frequency of shedding varies from 0.55% to 82%.[10–13] Importantly, the abundance of HSV-1 in asymptomatic individuals is low, with an upper median range of $10^4$ copies of HSV-1 DNA per mL saliva.[13 14] In contrast, in our patient with the burning mouth syndrome, there were $3.4\times10^8$ copies of HSV-1 DNA per mL saliva. The possibility exists that these very high viral DNA copy numbers reflected asymptomatic shedding; however, the copy number in our patient was 4 logs higher than the mean copy number in asymptomatic shedders. The fact that pain improved with antivirals along with the disappearance of HSV-1 DNA, further supports a causal link between HSV-1 and burning mouth syndrome in this patient.

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The patient's pain in the right V2–V3 distribution, including the right anterior 2/3 of anterior tongue, is consistent with the distribution of sensory afferent fibres from the trigeminal ganglion to the face and mouth, indicating that HSV-1 was reactivated from the right trigeminal ganglia. A similar pattern of facial pain and trigeminal ganglionitis has also been produced by VZV infection.[15] Meanwhile, the high load of salivary HSV-1 DNA and resolution of pain with antivirals demonstrate HSV-1 as the causative agent in this patient's burning mouth syndrome. Overall, HSV-1 infection should be considered in the differential diagnosis of burning mouth syndrome, particularly since it is eminently treatable with antiviral therapy. Future studies are needed to determine the frequency and abundance of HSV-1 in saliva of patients with burning mouth syndrome, as well as the benefits of antiviral treatment.

## Learning points

- Herpes simplex virus type 1 (HSV-1), with and without rash, can cause burning mouth syndrome.
- Diagnosis can be confirmed by the presence of high copy numbers of HSV-1 DNA in saliva.
- Treatment with valacyclovir rapidly alleviates pain.

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