

# Case Report: Recurrent Herpes and Post-traumatic Stress Disorder

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## KEY WORDS

■ RECURRENT HERPES ■ POST-TRAUMATIC STRESS DISORDER

■ ANXIETY DISORDERS ■ ANTIDEPRESSANTS

## SUMMARY

A 33-year-old male presented with recurrent outbreaks of perioral herpes of disfiguring nature that remained unresolved following therapy. The first perioral outbreak occurred following a road accident. The psychiatric interview conducted with the patient suggested post-traumatic stress disorder (PTSD) secondary to the accident. Venlafaxine 50 mg/day was initiated and led to resolution of the PTSD symptoms within 8 weeks. The patient did not experience any further herpes outbreaks for about 10 months. Control of stress disorders in recurrent herpes is discussed from a therapeutic perspective.

## Introduction

RECURRENT HERPES SIMPLEX VIRUS (HSV) labialis is a very common infection. Approximately 20–40% of the population will experience labial or perioral outbreaks of vesicular herpetic lesions.<sup>1</sup> The number of outbreaks varies widely, ranging from rare episodes to monthly or even more frequent recurrences. Such recurrences are exacerbated by triggers, which reactivate the dormant virus. Triggers may include: sun exposure, psychological stress, onset of menses, illness and physical trauma. Of these factors, emotional stress is often cited by patients with recurrent herpes as a significant factor in the recurrence of lesions.<sup>2,3</sup> Numerous studies examining the relationship between recurrent HSV1 and HSV2 and stress have indicated that stress is a factor in recurrent herpes disease,<sup>4–7</sup> but data on psychosocial stress as a predictor of outbreak (of HSV2) have been inconclusive.<sup>8,9</sup> More information is required on the possible links between mood states and recurrent herpes,<sup>10</sup> and also on the potential influence of persistent stressors and transient mood states on herpes labialis recurrences.<sup>11</sup>

Both topical and episodic antiviral treatments for recurrent herpes labialis have variable efficacy in reducing the duration of the signs and symptoms,<sup>12</sup> and prophylaxis treatment to control potential triggers should represent a new treatment approach.<sup>13</sup> This case report could contribute to the evidence supporting the treatment of stress disorders in the management of HSV labialis outbreaks.

## Case Report

A 33-year-old male with no previous psychiatric history presented with recurrent outbreaks of perioral herpes

that remained unresolved following therapy. The outbreaks followed 8–10-day cycles. The eruptions were preceded by a prodrome, such as generalized weakness, together with localized tingling and burning at the site of the infection. In the following 10 h, blisters would appear around the mouth, lips and sometimes the nostrils, spontaneously resolving after about 10 days and leaving no scarring. Vesicles were bilateral. The disfiguring nature of the outbreaks, together with their frequency (8–10 outbreaks annually over the previous 4 years), had repercussions in his workplace and represented a major psychological burden, which led him to consult us in December 2002. At that time, he was not on medication.

The patient was able to specify the first outbreak as occurring in September 1995, following a road accident leading to the death of the passenger in the car he was driving. This first episode of herpes labialis occurred as a perioral plaque. Other episodes followed, occasionally at first, then at increasingly frequent intervals. A dermatologist had made a clinical diagnosis of recurrent herpes labialis and had prescribed specific local and prophylactic antiviral chemotherapy (aciclovir), which was poorly tolerated (due to nausea); consequently, the therapy was taken irregularly and was inadequately effective over a period of 6 years. The patient's occupational physician referred him to us because the herpes labialis recurrences had major repercussions in his professional life (colleagues laughed at his facial appearance) and he took frequent sick leave. His occupational physician suggested a psychosomatic link to his recurrent herpes.

We conducted a psychiatric interview, which suggested post-traumatic stress disorder (PTSD):<sup>14</sup> exposed to a traumatic event during which he was seriously affected and where a close friend died, the patient was experiencing recurrent and intrusive distressing recollections of the accident, recurrent dreams reliving the accident, emotional blunting, irritability and sleeping disorders, and he attempted to avoid cues that might trigger the memory of the accident. He identified nocturnal periods of intense revival of the event as triggers for renewed outbreaks. The patient connected the herpes to the accident during the first consultation. Venlafaxine 50 mg/day was initiated to treat the PTSD and was supplemented with psychotherapy. This led to a resolution of the episodes of nocturnal revival of the trauma within 10 days, and resolution of the PTSD symptoms within 8 weeks. In parallel, the patient did not experience any recurrent herpes outbreaks for about 10 months, despite being exposed to events he described as short-term stressors (redundancy at work, becoming a father). After

10 months, the patient spontaneously stopped the treatment and experienced only two localized outbreaks of herpes labialis during the following 12 months.

## Discussion

Monthly recurrences of herpes labialis and cutaneous-mucosal herpes affect only a small number of patients. The severity of the illness is mostly mild, although it is uncomfortable and disfiguring. The handicapping consequences are aggravated by the fact that they are diffuse, often requiring prophylactic antiviral therapy. The psychological impact of a prominent facial infection, particularly in young patients with frequent or severe recurrences, should not be underestimated. Environmental factors, including stress, have been implicated in the onset of herpes labialis recurrences.<sup>15</sup> Two clinical studies have demonstrated that stressors enhance susceptibility and severity of the primary infection to a latent herpes virus as well as clinical recurrences.<sup>8,16</sup> Recent literature suggests that a range of diseases is influenced by immune modulation, such as by proinflammatory cytokines, the production of which can be directly stimulated by psychological stressors.<sup>17</sup> In particular, some neuroendocrine hormones, such as adrenaline, have been shown to influence macrophage-mediated lysis of HSV-infected cells.<sup>18</sup> In addition to stress, negative mood has also been investigated as a potential trigger for recurrences, but the findings were inconsistent.<sup>10,19</sup>

PTSD is a major persistent stress disorder, which has been associated with changes in the immune system, and this relationship may be mediated by the onset of sleep disturbances.<sup>20</sup> PTSD has also been shown to be associated with viral reactivation of HSV.<sup>21</sup> Somewhat surprisingly, the control of stress factors in recurrent herpes has not been discussed from a therapeutic perspective, particularly in relation to chemotherapy.<sup>12</sup> To the best of our knowledge, there have been no reports on the use of psychotropic medication to prevent herpes labialis recurrences other than lithium, which has been described as exerting a direct effect on the replication of HSV.<sup>22</sup> Venlafaxine is an antidepressant that has proven its efficacy in the treatment of PTSD.<sup>23</sup> In this case report, venlafaxine treatment was prescribed to reduce symptoms of PTSD, particularly recurrent dreams

reliving the accident, which were identified as a trigger for herpes labialis recurrences. The reduction of these stressful symptoms was associated with a reduction in the number of herpes labialis recurrences. The mechanism of action of venlafaxine in this case is unclear, but we suppose it has an indirect action by reducing chronic stress. Treatment of persistent stressors, such as PTSD with recurrent dreams, could contribute to a decreased frequency of herpes labialis recurrences, whereas the incidence of short-term stressors was not associated with such recurrences. It is also possible that psychotherapy contributed to the reduction in the number of herpes labialis recurrences and explained the absence of such recurrences before resolution of PTSD. In summary, the patient needed treatment for PTSD, and control of the herpes was a secondary benefit.

## Conclusion

This case suggests that it is possible to reduce the frequency of herpes labialis recurrences by treating chronic stress that is associated with the recurrences. Further studies should assess the role of persistent stressors or continuing high levels of anxiety (such as PTSD), which can be treated with specific therapies. If the specific action of venlafaxine is confirmed in future cases, prospective and randomized studies are needed to clarify the mechanism of action and potential indications of this psychotropic drug.

## Conflicts of Interest

No conflicts of interest were declared in relation to this article.

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## Key Paper

### CMV-hyperimmune globulin for preventing cytomegalovirus infection and disease in solid organ transplant recipients: a meta-analysis.

Bonaros N, Mayer B, Schachner T, Laufer G, Kocher A. *Clin Transplant* 2008;**22**:89–97.

CMV

**OBJECTIVE:** The goal of this meta-analysis was to investigate the impact of cytomegalovirus hyperimmune globulin (CMVIG) on cytomegalovirus (CMV) infection, CMV disease, and mid-term survival in solid organ transplant recipients. **METHODS:** Medline, EMBASE, and the Cochrane databases were searched since their inceptions until 2006. Inclusion criteria comprised: prospective randomized trials, in solid organ transplantation which received CMV prophylaxis including CMVIG on one of the treatment arms. Random effects models were used to calculate pooled risk ratios (RR) and meta-regression was employed to explain study heterogeneity. Stratified analyses were conducted and Funnel plot was used to assess publication bias. **RESULTS:** Literature searches identified 11 randomized trials (698 patients; median follow-up: 12 months, range: 3–22 months) including

six randomized trials (302 patients) after kidney transplantation. The analysis demonstrated a beneficial effect of the prophylactic use of CMVIG on total survival (RR [95% confidence interval; CI]: 0.67 [0.47–0.95]) and prevention of CMV-associated death (RR [95% CI]: 0.45 [0.24–0.84]) in solid organ transplant recipients but not kidney transplant recipients (RR [95% CI]: 0.35 [0.12–1.04]). CMV disease was significantly reduced in all recipients receiving prophylactic CMVIG (RR [95% CI]: 0.697 [0.57–0.85]). CMVIG had no impact on CMV infections and clinically relevant rejections. **CONCLUSIONS:** Prophylactic administration of CMVIG after solid organ transplantation is associated with improved total survival, reduced CMV disease, and CMV-associated deaths.

## Erratum

Breuer J, Whitley R. *Herpes* 2007;**14**(Suppl 2):25A–29A.

On page 28A, the fourth bullet point under the heading ‘Current Treatment of Herpes Zoster’ and the sixth bullet point under the heading ‘Recommendations and Statements’ read as follows: ‘Once-daily brivudin is an effective therapy for herpes zoster, although further evaluation is needed. Brivudin should be used only in

immunocompetent hosts as it has the potential to cause serious toxicity if co-administered with 5-fluorouracil’. This was incorrectly given a category 2 recommendation. The efficacy evidence from clinical trials actually supports a category 1 recommendation for this statement.