Concurrent Herpes Simplex Type 1 and Varicella-Zoster in the V2 Dermatome in an Immunocompetent Patient

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A unique feature of herpesviruses is their ability to establish latent infection within the nervous system by colonizing peripheral sensory ganglia, which results in subsequent episodic outbreaks of infection triggered by precipitating events. Despite the latent nature of both herpes simplex virus type 1 (HSV-1) and varicella-zoster virus (VZV) within these sensory ganglia, simultaneous outbreaks of these viruses are uncommon. This is generally attributed to the differing reactivation features of these 2 viruses. Four cases of concurrent HSV-1 and VZV infection are described in the literature. We report concurrent infection of HSV-1 and VZV within the same V2 dermatome in an immunocompetent patient.

Case Report

An 84-year-old man in good health was admitted to Columbia-Presbyterian Hospital for traumatic fracture of his lumbar spine at L2-3. His medical history included a non–small-cell lung cancer, which was surgically treated by lobectomy a few years previously. The patient had not required chemotherapy or radiation therapy, and his metastatic workup was negative. On admission for bed rest and physical therapy, he was alert and oriented, complaining only of low back pain. On the tenth hospital day, he appeared confused and drowsy and developed an area of erythema on the right cheek and upper lip. He was treated empirically for cellulitis with cefazolin.

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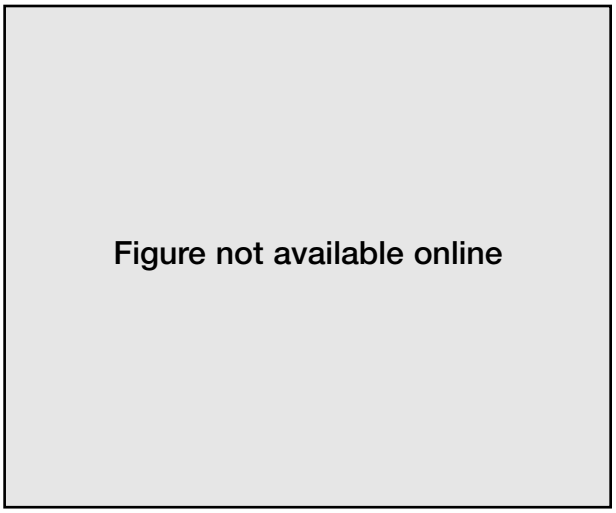

Multiple vesicles over the lip, cheek, and nose in the V2 dermatome. Varicella-zoster virus was detected in these lesions.

No improvement was seen after 4 days of antibiotic therapy, and a dermatology consultation was obtained. The patient was febrile (38.5°C), confused, and minimally responsive. His right cheek and upper lip were swollen with a unilateral eruption of multiple erythematous, superficial, thin-walled vesicles over the right V2 dermatome, sharply demarcated at the facial midline. The right side of the patient's hard palate was raised, diffusely erythematous, and covered with a white exudate that stopped at the midline (Figure). Swabs of both the facial vesicles and palatal region were obtained and sent for viral cultures and direct fluorescent antibodies. The facial vesicles were found to be negative for HSV-1 and positive for VZV. Both viral cultures and direct fluorescent antibodies of the hard palate were positive for HSV-1 and negative for VZV. The results were repeated and confirmed.

He was treated with intravenous acyclovir 400 mg every 8 hours. Over the next 2 days, his mental status improved slightly, and the facial vesicles began to encrust. By the third day of treatment, his mental status once again deteriorated, and a lumbar puncture was performed. The cerebrospinal fluid (CSF) was found to have a glucose level of 51 mg/dL; protein of 51 mg/dL; 10/mm^3 red blood cells; 30/mm^3 white blood cells (WBC), with 13% neutrophils, 86% lymphocytes, and 1% monocytes. The peripheral glucose was 92 mg/dL, and the WBC was 8.2×10^9/L. The elevation of CSF protein and the lymphopleocytosis suggested herpes encephalitis. An electroencephalogram demonstrated diffuse background slowing, consistent with a pattern of nonspecific encephalopathy. Magnetic resonance imaging of the head, with and without contrast, revealed no enhancement of the leptomeninges and was otherwise noncontributory. All CSF cultures, including bacterial, fungal, cryptococcal and acid-fast bacilli, were negative. No viral cultures were obtained.

His facial and palate lesions resolved, but his course was complicated by recurrent episodes of bacterial pneumonia and a worsening of his mental status. He died on hospital day 90. No postmortem was performed.

Comment

Both HSV-1 and VZV are members of the α-Herpesviridae subfamily. Common features of this family include sensory neurotropism and the ability to move between latent sites in the sensory ganglia and the corresponding innervated epidermis.[1] Despite these similarities, several important differences between these viruses make concomitant viral outbreaks uncommon. Such differences include rates of viral reactivation, frequency of viral reactivation, factors that trigger viral reactivation, and histologic sites of viral latency.

The rates of reactivation of HSV and VZV differ considerably. In 1992, Meier and Straus,[1] analyzing data from a population-based study, found that although VZV seropositivity in the general population is greater than 90%, the estimated lifetime risk of herpes zoster is between 10% and 20%.[1,2] Additionally, they found that VZV usually reactivates only once and rarely more than once (3.9%). In contrast, a seroepidemiologic study found that the incidence of HSV-1 seropositivity approaches 90% by age 60 years and that reactivation will occur in more than half of infected persons (as often as several hundred times in a lifetime.)[3]

Timing of reactivation also differs between HSV and VZV. Of significance, VZV reactivation is associated with advancing age, whereas HSV reactivation occurs more frequently in the young and declines throughout life. Antibody titers to VZV are similar in both young and old patients, but a marked decline in cellular immune response to the VZV antigen occurs in the older population (>60 years) while normal cellular responses to other antigens are maintained.[4,5] In contrast, Corey and Spear[6] reported that HSV reactivation appears more frequently in the first years after initial infection and decreases over time. They suggest that this finding is consistent with a developing immune response, which serves to suppress subsequent infection.[6]

The inducing stressors are thought to differ among these viruses. VZV reactivates in the presence of trauma and x-ray, but does not seem to have a predictable response typical of HSV reactivation, which tends to occur in settings of emotional and physical stress, immunosuppression, ultraviolet light exposure, and direct facial trauma.[7] Molecular analysis suggests that stimuli trigger various neuronal transcription factors such as c-fos and c-jun, which alter gene expression, leading to increased viral replication of HSV.[8] In contrast, little is known about molecular regulation of VZV reactivation.[9]

Meier and Straus[1] also have proposed a model to explain the various rates of reactivation of HSV versus VZV based on the site of viral latency. This model is based on data[9] that suggests that HSV resides in the neuronal cell itself, and therefore is more easily stimulated and more frequently reactivated. In addition, it is believed that during reactivation, interneuronal viral spread within a ganglion may account for the occasional zosteriform presentation of HSV, as was seen in our patient.[10] In contrast, VZV resides in the more distant satellite cells of the sensory nerve ganglion and is therefore less easily activated, requiring intracellular signals beyond direct sensory nerve stimulation. VZV reactivation has been noted to occur following persistent nerve stimulation, resulting in cell-cell spread of the virus, precipitating severe tissue damage, neuralgia, and zoster.[7]

Although simultaneous reactivation of HSV and VZV are uncommon, such outbreaks have been reported in the literature in immunocompromised patients. Kahn[11] reported VZV in the V3 dermatome and HSV of the sacroiliac region in a woman with tuberculosis. Cupps et al[12] reported recurrent simultaneous disseminated VZV, perineal HSV-2, and pulmonary cytomegalovirus (CMV) in a woman with acquired immunodeficiency syndrome (AIDS); and Gibney et al[7] reported oral (lips and hard palate) HSV and sacral VZV in a kidney transplant patient. Binet et al[13] demonstrated HSV and VZV of the left side of the thorax and HSV of the perineum,

followed by HSV of the left hand in a 22-year-old woman with normal immune response.

Reports of other concomitant cutaneous DNA viral infections include Smith et al[14] who reported involvement by both CMV and HSV in 2 patients infected with human immunodeficiency virus. Penneys and Hicks[15] reported cases of disseminated VZV and disseminated CMV with localized HSV, in the AIDS population.

We report the first case of concomitant cutaneous HSV-1 and VZV infection involving the V2 dermatome in an immunocompetent host. Additionally, we report an unusual zosteriform midline demarcation in the hard palate, which is not commonly seen in HSV-1. Although the molecular stimuli for reactivation of both HSV and VZV remain to be elucidated, our case suggests that a common triggering event may exist that allowed both HSV and VZV to be reactivated simultaneously from the same sensory ganglion. This process of interganglionic viral replication also may explain the unusual zosteriform presentation of HSV in our patient.

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