Herpes simplex virus infection presenting as a piriform sinus mass

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Abstract
Evidence is accumulating that herpes simplex virus (HSV) infection is implicated in oncogenesis. HSV antigens have been observed in some oral cancers. We present the case of a 62-year-old man who presented with dysphagia, odynophagia, and dysphonia and who was found on computed tomography (CT) to have a mass in his piriform sinus. We suspected a malignancy, but histopathology of biopsy specimens revealed that the mass exhibited the classic signs of the HSV cytopathic effect, including the presence of intranuclear inclusion bodies, ballooning degeneration of epithelial cells, and a ground-glass appearance of some nuclei. The patient responded well to antiviral therapy, and posttherapy CT revealed that the mass had resolved completely. To the best of our knowledge, this is the first report in the literature of a case of HSV infection presenting as a piriform sinus mass.

Introduction
Herpes simplex virus (HSV) is one among a spectrum of viruses known to affect the upper aerodigestive tract, although it is usually confined to the lips and oral cavity. It is transmitted via saliva, and it can produce a constellation of symptoms in its host that range from vague malaise to life-threatening illness. There is increasing evidence that the virus contributes in various steps along the carcinogenic cascade. In fact, HSV antibodies are elevated in some patients with oral cancer. In this article, we describe a case of HSV infection that manifested as a mass in the piriform sinus. To the best of our knowledge, this is the first such case to be reported in the literature.

Case report
A 62-year-old man presented to the emergency room with a 7-day history of dysphagia and odynophagia and a 3-day history of dysphonia. Several days prior to presentation, he had been placed on antibiotics, but his symptoms persisted. His medical history was significant for gastroesophageal reflux and chronic obstructive pulmonary disease. Previous surgeries included a cholecystectomy, appendectomy, and bilateral total knee arthroplasties. His social history was significant for both tobacco (40 pack-years) and alcohol (several beers per day). Laboratory studies were grossly normal. A lateral x-ray of the soft tissues of the neck was read as demonstrating a rounded area of density in the subglottic region. The patient was admitted, and the otolaryngology service was consulted.

Physical examination revealed that the patient appeared to be generally healthy and in no acute distress. He was afebrile, and his vital signs were stable. His oral mucosa was devoid of any abnormalities. His nares demonstrated mild rhinitis with clear rhinorrhea. There was no sinus tenderness to palpation. Examination of the neck did not reveal any adenopathy or thyromegaly, and his tracheal structures were in the midline. Findings on the otologic examination were unremarkable. Flexible nasopharyngoscopy demonstrated a fullness in the left piriform sinus with no exophytic changes. His vocal folds were mobile, and his airway was adequate.

Computed tomography (CT) detected a 2-cm mass in the left piriform sinus with some impingement on the hypopharynx (figure 1). Magnetic resonance angiography was obtained to investigate the possibility of a vascular parapharyngeal contribution, and it demonstrated parapharyngeal asymmetry with fullness and heterogeneity of the left tonsillar pillar, vallecula, and piriform sinus. The patient was taken for direct laryngoscopy. On examination with a Jackson laryngoscope, there were no mucosal abnormalities, but a generalized fullness of the left piriform sinus and vallecula was observed, as well as some fullness of the lingual tonsils and faucial pillars. Several biopsies were taken.

Based on the patient’s risk factors, we suspected a squamous cell cancer, but biopsies of the apparent tumor...
were unexpectedly negative for malignancy. Instead, histopathology of specimens taken from the left piriform sinus, left aryepiglottic fold, left vallecula, and left tonsillar pillar demonstrated a viral cytopathic effect and necrosis consistent with HSV infection. Signs of the classic HSV cytopathic effect included the presence of intracellular proteinaceous fluid, ballooning degeneration of epithelial cells, and acantholysis (figure 2, A) as well as intranuclear inclusion bodies and a ground-glass appearance of some nuclei (figure 2, B). Also identified were several zones of coagulative necrosis. None of the specimens exhibited dysplasia, granuloma, or malignancy.

The patient was started on intravenous acyclovir and tested for human immunodeficiency virus (HIV). He responded well to the antiviral medication, and his symptoms resolved completely. We do not know whether the piriform sinus mass actually represented just a localized inflammatory reaction instigated by the viral infection, but follow-up CT revealed that it too had resolved completely after antiviral therapy. Results of the patient’s HIV serum antibody test were negative, and he was discharged home on valacyclovir.

Discussion

The features of this case bring to mind the increasing evidence of a link between viral infection and malignancy of the head and neck. Of note, our patient had risk factors for developing a malignancy, which may further implicate HSV in the development of squamous cell carcinoma. First, our patient’s demographic characteristics placed him at a higher risk of developing a malignancy. Second, he compounded his risk by regularly using both tobacco and alcohol. In fact, studies have demonstrated that herpesvirus acts synergistically with tobacco to produce oral cancer in animals. It is possible that cigarette smoking predisposes patients to mucosal HSV infection by suppressing the host defenses, such as natural killer cell activity, that are required to control HSV.

The HSV genome itself has been found to have distinct transforming regions. Park et al demonstrated that immunization against HSV prevented the co-carcinogenic activity of the virus with the oral carcinogen dimethylbenzanthracene. Additional evidence of a viral link to carcinogenesis was provided by the discovery that serum antibodies to HSV are elevated in patients with head and neck cancer.

Although viruses are unlikely to be the prime agents involved in the etiology of oral cancer, mechanisms do exist that allow viral DNA or its gene products to act at different stages along the carcinogenic cascade. This theory is consistent with the multifactorial process of cancer development. We must be mindful of these associations when treating our head and neck cancer patients.

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