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Case Report

Herpes simplex virus bronchiolitis in a cannabis user

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ABSTRACT

Herpes simplex virus (HSV) lower respiratory tract infections in adults are uncommon. We present a case of HSV bronchiolitis and pneumonitis in an immunocompetent individual, likely linked to chronic habitual marijuana use and a herpetic orolabial ulcer. The case serves as a reminder to consider HSV as a potential unusual cause of lower respiratory tract infection/inflammation in individuals with chronic habitual marijuana use.

Introduction

Herpes simplex virus (HSV) is a double-stranded DNA virus with two strains, HSV-1 and HSV-2. After primary infection, herpesviruses establish a life-long latent infection through persistence in neurons of the dorsal root ganglia and the autonomic nervous system [1]. Reactivation can be triggered by local and systemic factors (*e.g.* ultraviolet irradiation, tissue damage, fever, physical or emotional stress, immunosuppression). Some common clinical manifestations of HSV-1 infection include gingivostomatitis (primary infection), herpes labialis, encephalitis, and keratoconjunctivitis.

HSV-1 can often be recovered from bronchial secretions, especially in intubated patients [2,3]. However, true HSV-1 lower respiratory tract infections in immunocompetent adults are uncommon. We present a case of a HSV-1 lower respiratory tract infection likely linked to marijuana inhalation at the time of an active herpetic orolabial ulcer.

Case

A 46-year-old male initially presented with a 1 week history of fevers, headache, non-productive cough, and increasing dyspnea. He was admitted to the hospital and treated with antibiotics, bronchodilators and intravenous and oral corticosteroids for presumed community-acquired pneumonia and asthma exacerbation. He was discharged and completed a 10 day course of antibiotics and an oral prednisone taper without significant improvement in his symptoms. He returned for medical care 2 weeks after illness onset with continued fevers, malaise, and dyspnea with minimal exertion and a persistent non-productive cough with post-tussive emesis.

His past medical history included mild asthma, no inhaled or chronic systemic corticosteroid use, and only occasional use of albuterol metered dose inhaler; Hepatitis C, treated with Interferon-alpha/Ribavirin and achieved sustained virological response 6 years prior to admission; and depression. His medications were Cefpodoxime; he had completed an oral prednisone taper 2 days prior to admission.

The patient was an unemployed construction worker, married with 4 children. He had a distant history of crack cocaine use and IV heroin use. He was a chronic habitual marijuana smoker, 3–5 times per week. The patient quit tobacco 4 years earlier and had a 20 pack-year history. He was born in Puerto Rico and came to the U.S. mainland as an infant. There had been no recent travel and he had one dog at home.

On physical examination, the patient's temperature was 36.3 °C. The blood pressure was 122/70 mmHg, pulse 60 beats per minute, respirations 20 breaths per minute, and oxygen saturation 96% on 3 l oxygen nasal prong.

The patient had evidence of a healed ulcer on the lateral aspect of his left upper lip. There were no active ulcerations noted over the lips, anterior, or posterior oropharynx.

The patient had bilateral rhonchi over the mid posterior lung fields and late expiratory wheezing with forced expiration

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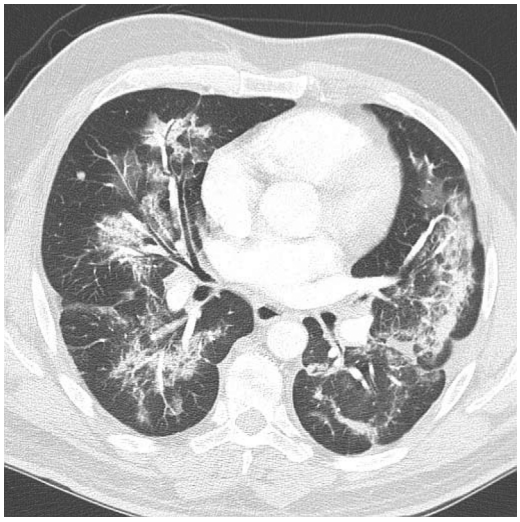

Fig. 1. Chest CT scan image. Bilateral bronchial wall thickening and ground glass opacities in a peri-bronchovascular distribution.

bilaterally. There were no rales. The remainder of the exam was unremarkable. The white blood cell count was 18,900/mm^3 with 65% neutrophils, 20% lymphocytes, 11% monocytes, 3% eosinophils, and 1% basophils. HIV ELISA test was negative. A CT scan of the chest with pulmonary embolism protocol revealed no pulmonary embolism, but demonstrated bilateral bronchial wall thickening, and ground glass opacities in a peri-bronchovascular distribution (Fig. 1).

The patient was begun on vancomycin and piperacillin/tazobactam, intravenous methylprednisolone, bronchodilators, and supplemental oxygen. Routine blood cultures obtained on admission were negative. Urine antigens for *Legionella* sp. and *Streptococcus pneumoniae* were negative. An expectorated sputum culture grew normal upper respiratory flora. After 2 days, the patient had not clinically improved and he underwent a bronchoscopy with bronchoalveolar lavage and transbronchial biopsy. There were no endobronchial masses, ulcers, or hemorrhage seen. The biopsy specimen revealed chronic interstitial pneumonitis, squamous metaplasia and herpetic viral inclusions in bronchial epithelial cells (Fig. 2a). Immunostaining was positive for HSV-1 (Fig. 2b), and negative for respiratory syncytial virus and cytomegalovirus. A diagnosis of HSV bronchiolitis and pneumonitis was made. The bronchoalveolar lavage viral culture grew herpes simplex virus. Bacterial, mycobacterial, and fungal cultures from the bronchoscopy specimens were unremarkable. The patient also had a positive anti-HSV IgM antibody level, an elevated anti-HSV-1 IgG titer, and negative anti-HSV-2 IgG titer.

Upon additional questioning, the patient recalled that he had a large herpetic ulcer on his left upper lip for 1–2 weeks approximately 1 month prior to his initial presentation. He had continued to regularly smoke marijuana through a pipe while having the orolabial ulcer. He was treated with intravenous acyclovir every 8 h and continued methylprednisolone. The antibiotics were discontinued. After several days of treatment and clinical improvement, he was switched to oral famciclovir every 8 h for a total of 4 weeks along with a slow oral prednisone taper. He was seen in follow-up 3 weeks after discharge and he reported near complete resolution of symptoms.

Discussion

HSV lower respiratory tract infections in adults are uncommon. HSV tracheobronchitis and pneumonitis have been typically described in immunocompromised individuals: burn patients, pregnancy, HIV, malignancy, as well as solid organ and hematopoietic stem cell transplant recipients [4–6]. We present a case of HSV bronchiolitis and pneumonitis in an immunocompetent individual, likely linked to chronic habitual marijuana use. The histopathology from the transbronchial biopsy and the positive anti-HSV IgM serology support acute invasive infection and not simply colonization. We postulate that chronic marijuana use led to squamous metaplasia in the bronchioles. The squamous metaplasia from chronic marijuana use likely promoted localized viral replication in the lower respiratory tract [7]. Squamous epithelial cells are a permissive cell type for HSV replication, and previous reports have highlighted that HSV has nearly always been seen in areas of squamous metaplasia in lower respiratory tract infections [8]. Marijuana smoking with deep inhalations at the time of the orolabial herpetic ulcer promoted deep tracheobronchial seeding of HSV. The combination of these two factors led to the HSV bronchiolitis and pnemonitis. A few cases of HSV esophagitis and pneumonitis have been reported among immunocompetent patients with HSV orolabial ulcers [9,10]. Tobacco smoking has been associated with an increased risk for community acquired pneumonia and influenza [11]. Marijuana smoking has been associated with an increased risk for acute and chronic bronchitis [12].

Additional undefined intrinsic host factors, and localized immune and inflammatory changes in the respiratory tract produced by chronic habitual marijuana use, may have also contributed to the development of HSV bronchiolitis and pneumonitis. The short-term corticosteroid use before the second admission may have also played a role. This case serves as a

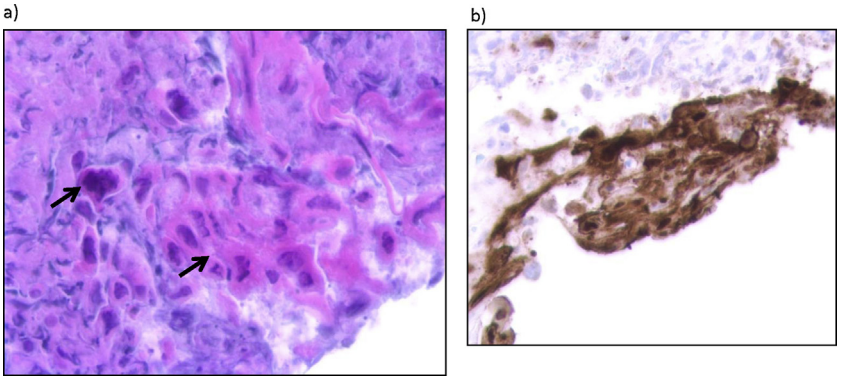

Fig. 2. Histopathology from transbronchial biopsy. (a) Herpes virus inclusion bodies and cytopathic effect (arrows) with necrosis in bronchial wall tissue (H&E stain, 400× magnification). (b) Immunoperoxidase staining for herpes simplex virus-1 (HSV-1) (brown color) in surface bronchial epithelial cells (400× magnification).

reminder to consider HSV as a potential unusual cause of lower respiratory tract infection/inflammation in individuals with chronic habitual marijuana use.

Conflict of interest

None.

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