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Pneumomediastinum and Pneumothorax Associated with Herpes Simplex Virus (HSV) Pneumonia

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Male, 37
Final Diagnosis: HSV pneumonia
Symptoms: Cough • fever • sob
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases

Objective: Unusual clinical course

Background: Pneumonia is one of the most common causes of death from infectious disease in the United States (US). Although most cases of community-acquired pneumonia (CAP) are secondary to bacterial infection, up to one-third of cases are secondary to viral infection, most commonly due to rhinovirus and influenza virus. Pneumonia due to herpes simplex virus (HSV) is rare, and there is limited knowledge of the pathogenesis and clinical complications. This report is of a fatal case of HSV pneumonia associated with bilateral pneumothorax and pneumomediastinum.

Case Report: A 36-year-old homeless male Hispanic patient, who was a chronic smoker, with a history of intravenous drug abuse and a medical history of chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection, not on highly active antiretroviral therapy (HAART), was admitted to hospital as an emergency with a seven-day history of productive purulent cough. The patient was admitted to the medical intensive care unit (MICU) with a diagnosis of CAP, with intubation and mechanical ventilation. Broncho-alveolar lavage (BAL) was performed and was positive for HSV. The patient developed bilateral pneumothorax with pneumomediastinum, which was fatal, despite aggressive clinical management.

Conclusions: Pneumonia due to HSV infection is uncommon but has a high mortality. Although HSV pneumonia has been described in immunocompromised patients, further studies are required to determine the pathogenesis, early detection, identification of patients who are at risk and to determine the most effective approaches to prophylaxis and treatment for HSV pneumonia.

MeSH Keywords: Herpes Simplex • Pneumomediastinum, Diagnostic • Pneumonia, Viral • Pneumothorax

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/906051>

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Background

Pneumonia is defined as an infection of the parenchyma of the lung and is also referred to as lower respiratory tract infection. In 2014, the National Center for Health Statistics in the US reported that pneumonia was the eighth cause of mortality [1]. Viruses are the third most common cause of community-acquired pneumonia (CAP) [2]. Herpes simplex virus (HSV) can cause infection of the upper and lower respiratory tract, with upper airway infection due to HSV being relatively common, with an incidence ranging from 6–12% [3]. However, HSV infection of the lower respiratory tract, or HSV pneumonia, is rare and is usually an opportunistic infection [4].

Although the precise incidence of HSV pneumonia remains to be determined, autopsy studies have estimated that the incidence of lower respiratory tract HSV infection in unselected patients was 0.5%, and was associated with critically ill patients, including patients with burn injuries and prolonged intubation [5]. One published study of a small number of cases has shown that the patient mortality in HSV pneumonia is 100% [6]. Despite the low incidence and high mortality, prophylaxis for HSV infection in susceptible patients is not currently indicated. However, previously published studies have shown that prophylaxis reduces the incidence of HSV pneumonia in patients with acute respiratory distress syndrome (ARDS), and a reduction in mortality in patients who are hospitalized in intensive care units (ICUs) [5,7].

There are three ways in which HSV can reach the lower respiratory tract from the upper respiratory tract: by contiguous spread, by aspiration, or by viral shedding. HSV infection of the lower respiratory tract can be associated with necrotizing pneumonitis, and diffuse pneumonia. Pneumothorax and pneumomediastinum, although uncommon complications, should be monitored due to the associated high patient mortality [8]. This report is of a fatal case of HSV pneumonia associated with bilateral pneumothorax and pneumomediastinum.

Case Report

A 36-year-old male Hispanic patient, who was a chronic smoker, with a history of intravenous drug abuse and a medical history of chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection, diagnosed ten years previously, was admitted to hospital as an emergency with a seven-day history of productive purulent cough. For the previous two years, the patient was homeless and was unable to afford the high cost of highly active antiretroviral therapy (HAART). The patient's family history was unremarkable, but his social history was that he was a homeless, single, sexually active male with several previous sexual partners and no known drug allergies. The

patient was in his usual state of health until one week before admission to the hospital emergency department.

On hospital admission, the patient complained of progressive and constant productive cough with yellow sputum, associated with dysphagia, general malaise, fever, night sweats, chills, shortness of breath, nausea, and a three-month history of weight loss of approximately 40 lbs. His vital signs on admission to hospital included a blood pressure (BP) of 105/60 mmHg, respiratory rate (RR) of 27 per minute, heart rate (HR) of 116 beats per minute (bpm), temperature of 38.8°C, pulse oximetry of 81%, and the fraction of inspired oxygen (FiO₂) of 0.21.

Physical examination showed that the patient's height was 66 inches and his body weight was 120 pounds (ideal body weight, 140.7 pounds). He had appeared to be acutely ill, in obvious respiratory distress, with poor dentition and with loosely attached white patches on the tongue, consistent with oral candidiasis (thrush). The trachea was in the midline. On lung auscultation, there were bilateral decreased breath sounds at both at the apex of both lungs and at both bases, with mild bilateral expiratory crackles.

The results of laboratory investigations performed in the emergency room showed leukopenia, hyponatremia, prerenal azotemia, a negative rapid influenza virology test and negative pneumococcal urinary antigen test; arterial blood gases (ABG's) taken in the emergency room showed decreased PaO₂/FiO₂, his alveolar-arterial (A-a) gradient was >35 mmHg and his pO₂ was <75 mmHg (Tables 1, 2). Anteroposterior (AP) chest X-ray images showed preserved cardiophrenic and costophrenic angles with a diffuse interstitial pattern of 'ground glass' opacities and perihilar thickening (Figure 1). Chest computed tomography (CT) scan without contrast was performed, which also showed bilateral 'ground glass' lung opacities (Figure 2).

The patient underwent the following severity scores for community-acquired pneumonia (CAP): Confusion, Urea, Respiratory rate, Blood pressure and age ≥65 yrs (CURB-65) score of 2 (predicted mortality of 14%); Pneumonia Patient Outcomes Research Team (PORT)/Pneumonia Severity Index (PSI) (1996) score of Class IV (predicted mortality of 8.2–9.3%); the Systolic blood pressure, Multilobar infiltrates, Albumin, Respiratory rate, Tachycardia, Confusion, Oxygen and pH (SMART-COP) score of 7, all met the criteria for severe pneumonia.

The patient was initially diagnosed with CAP and suspected Pneumocystis pneumonia (PCP). He was admitted to the medical intensive care unit (MICU) with a nasal cannula delivering oxygen at 3L/min and intravenous (IV) normal saline solution delivered at 125 ml/hr with no need for vasopressors. Initially, antimicrobial treatment included vancomycin 1,000 mg IV every 12 hours and piperacillin/tazobactam 4.5 grams IV every 6

Table 1. Laboratory investigations.

Laboratories	
White blood cell	3.8×10 ⁹ /L
Hemoglobin	9.8 gm/dL
Hematocrit	27.8%
Platelets	86×10 ⁹ /L
Sodium	129 mmol/L
Potassium	3.6 mmol/L
Chloride	99.00 mmol/L
CO ₂	24.00 mmol/L
BUN	28 mg/dL
Creatinine	1.2 mg/dL
GFR by Cockcroft-Gault	76.4 mL/min
BUN/CREA ratio	23.33
LDH	317 UI/L

Table 2. The findings of the measurement of the arterial blood gases (ABGs).

ABG's	
pH	7.348
pCO ₂	43.9 mmHg
pO ₂	58 mmHg
HCO ₃	23.1 mmol/L
O ₂ sat	83%
Expected A-a gradient	13.0 mmHg
A-a gradient	36.7 mmHg
PaO ₂ /FiO ₂	276 mmHg

hours. Because PCP was suspected, he was treated with sulfamethoxazole/trimethoprim 250 mg IV every 6 hours. Given his A-a gradient and pO₂ findings, prednisone 40 mg twice daily was prescribed.

On the following morning, which was the second day of hospital admission, during the medical rounds, the patient's condition worsened, with sudden onset of severe respiratory distress, despite treatment with oxygen by nasal cannula. Subcutaneous emphysema was noted, and a decision was made to intubate the patient using orotracheal intubation, which was successful in the first attempt. The patient was placed on continuous mandatory ventilation (CMV) mode, with a tidal volume of 7 mL/kg and a positive end-expiratory pressure (PEEP) of 5 cm H₂O.

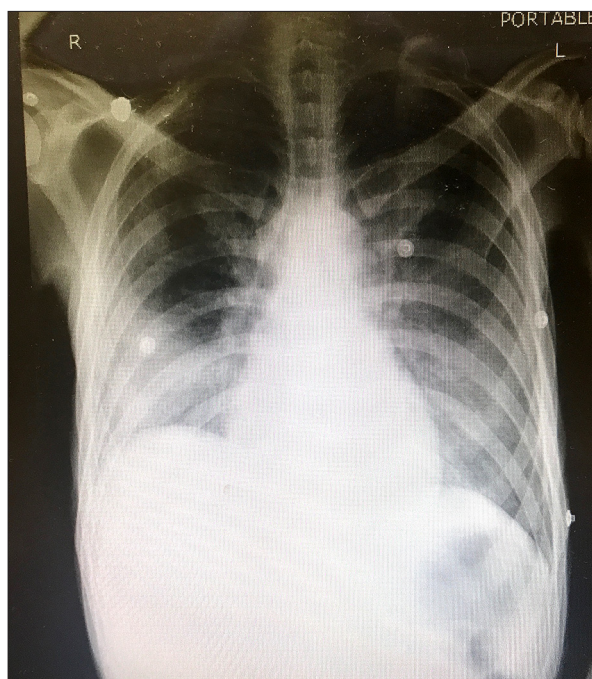


Figure 1. Anteroposterior (AP) chest X-radiograph. Chest X-ray shows a diffuse interstitial pattern of pneumonia with 'ground glass opacities' and perihilar thickening.

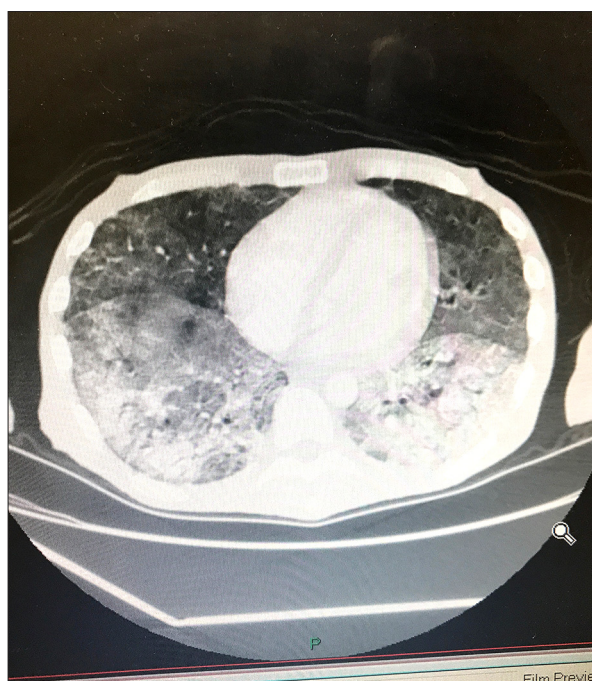


Figure 2. Chest computed tomography (CT) scan (without contrast). The chest computed tomography (CT) image shows bilateral 'ground glass' opacities, consistent with herpes simplex virus (HSV) pneumonia.

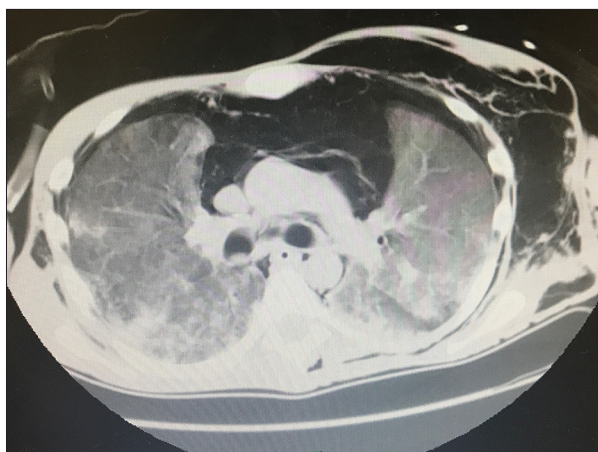


Figure 3. Chest computed tomography (CT) scan immediately following intubation. The chest computed tomography (CT) image shows bilateral pneumothorax and pneumomediastinum.

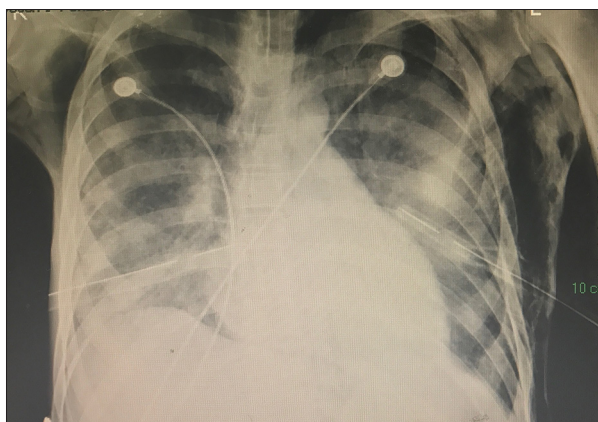


Figure 4. Chest X-radiograph showing the bilateral chest tubes. Chest X-ray shows bilateral chest tubes insertion.

A chest CT scan was requested immediately after intubation, which showed large bilateral pneumothorax (>3 cm from the chest wall to the lung parenchyma) and pneumomediastinum, requiring the insertion of bilateral chest tubes (Figures 3, 4). Pulmonary physicians recommended protective lung ventilation to avoid possible further bronchopleural fistula formation and to decrease air leaks. The clinical recommendations included the reduction of PEEP to 2 cm H₂O and reduction of respiratory tidal volume to 6 mL/kg.

Bronchoscopy was performed on the same day of intubation, and bronchoalveolar lavage (BAL) was positive for herpes simplex virus (HSV) only. Following consultation with the infectious diseases specialists, treatment commenced with IV acyclovir at 10 mg/kg every 8 hours. Blood culture, sputum culture, and BAL failed to demonstrate the presence of other pathogens.

However, despite the insertion of bilateral chest tubes, antibiotic therapy, treatment for PCP, and the use of protective

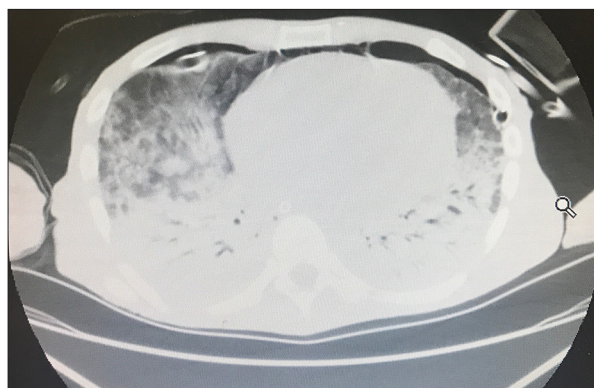


Figure 5. Repeat chest computed tomography (CT) scan. The repeat chest computed tomography (CT) image shows some reduction in the size of the pneumothorax and pneumomediastinum.

ventilation parameters, the patient's clinical continued to deteriorate, and he developed severe acute respiratory distress syndrome (ARDS), with a reduction of the initial PaO₂/FiO₂ from 276 mm Hg to 96 mm Hg. Further laboratory investigations remained unchanged, and a newly ordered brain natriuretic protein (BNP) was normal at 83 ng/ml. The repeat pulmonary CT scan showed a reduction of the previous pneumomediastinum and pneumothorax (Figure 5). Although extracorporeal membrane oxygenation (ECMO) was considered, this form of treatment was unavailable at our hospital, and the patient died.

Discussion

This report is of a case of herpes simplex virus (HSV) pneumonia associated with acute respiratory failure due with spontaneous air leak causing pneumothorax and pneumomediastinum, which was initially demonstrated by the presence of subcutaneous emphysema. Imaging studies were not performed immediately on hospital admission because the priority was to follow the ABC protocol of airway, breathing, circulation. Orotracheal intubation was a non-traumatic procedure and was successful at the first attempt. Although an initial diagnosis of Pneumocystis pneumonia (PCP) was made, examination of the sputum and bronchoalveolar lavage (BAL) failed to show Pneumocystis or any other infectious organisms and was positive only for HSV.

BAL has a sensitivity and specificity of 90% and 97%, respectively, for the diagnosis of bacterial pneumonia, and in this case, BAL was able to rule out bacterial infection [9]. The medical staff diagnosed acute respiratory distress syndrome (ARDS), rather than cardiac failure, which was supported by a negative brain natriuretic protein (BNP), absent cardiac gallop, S₃, jugular vein distention or hepatojugular reflux. Also, the findings from the PaO₂/FiO₂, in this case, fulfilled the current Berlin criteria for ARDS [10].

Before the development of antiretroviral drugs, opportunistic infections were the most common cause of death in patients with human immunodeficiency virus (HIV) infection. As in this case, the effect of lack of treatment for a patient with HIV, the likely decrease in the CD4 count, and a weakened immune system increases the risk of developing opportunistic infections. In the US, PCP, tuberculosis, and recurrent bacterial pneumonia are three of the ten most frequent acquired immunodeficiency (AIDS)-defining disease associations, with PCP increasingly reported in some areas of the world [11]. *Coccidioides immitis* and *Histoplasma capsulatum* are significant HIV-associated infections, and cytomegalovirus (CMV) and *Toxoplasma gondii* are the most frequent HIV-associated viral and parasitic infections reported, respectively [12].

HSV pneumonia in immunocompromised patients with HIV infection is not commonly recognized, and the incidence of HSV pneumonia in unselected patients has been reported to be 0.5% [5]. Despite previous reports of HSV pneumonia, the true incidence remains unknown, and there are no distinct clinical pathognomonic features of HSV pneumonia, as the presence of parenchymal ground-glass opacities and septal thickening are non-specific [12]. In 2007, a study in nonimmunocompromised patients showed that HSV bronchopneumonitis was a common finding in patients who deteriorated during prolonged mechanical ventilation (21%), possibly due to reactivation of HSV or infection from the mouth or throat, and was associated with poor clinical outcome [13]. However, bilateral pneumothorax and pneumomediastinum is not a common finding in HSV pneumonia.

Conclusions

There is no clear consensus regarding whether herpes simplex virus (HSV) is a primary pathogen or an opportunistic infection in pneumonia. For example, HSV pneumonia has been

described in nonimmunocompromised patients who are ventilated for more than five days [13]. Despite the high mortality of HSV pneumonia, there are no clinical recommendations for the use of antiviral prophylaxis, and although a small recent study has linked the reduction in mortality with acyclovir prophylaxis, no controlled clinical trials have yet been undertaken [7].

Several limitations in the clinical approach to diagnosis in this case are recognized. First, HSV pneumonia was diagnosed with BAL because the patient was critically ill, but a lung biopsy may have provided more information. Also, physical findings were highly suspicious for air leak before orotracheal intubation and ventilation. Furthermore, an autopsy was not performed, and so barotrauma as a cause of air leak cannot be completely excluded. Finally, two additional clinical tests that could have been included were a drug screen and a *Legionella* antigen test. Pneumonia due to HSV infection is uncommon but has a high mortality. Although HSV pneumonia has been described in immunocompromised patients, further studies are required to determine the pathogenesis, early detection, identification of patients who are at risk and to determine the most effective approaches to prophylaxis and treatment for HSV pneumonia.

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Conflict of interest

None.

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