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CASE REPORT

Diagnostic Dilemma of Herpes Simplex Virus Type 1 Pneumonia or Colonization: A Case Report

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Abstract: Herpes simplex virus type 1 (HSV1) pneumonia presents diagnostic challenges due to there being no gold-standard criteria currently. Specimens from bronchoalveolar lavage can increase specificity, and cytohistological examination can prove virus infection. Patients with high viral load have been reported with poor outcomes and benefited from antiviral agent. We describe an 80-year-old man with severe pneumonia who initially showed improvement without antiviral therapy, despite viral inclusion bodies on sputum cytology and positive HSV1 polymerase chain reaction from sputum, though subsequent clinical deterioration due to *Pseudomonas aeruginosa* infection necessitated intensive care. This case highlights the complexities of diagnosing and managing HSV1 pneumonia, emphasizing the importance of integrating clinical suspicion, radiological imaging, and laboratory tests for timely therapeutic decisions in critically ill patients.

Keywords: herpes simplex virus type 1, pneumonia, sputum cytology, polymerase chain reaction, antiviral therapy

Introduction

Herpes simplex virus type 1 (HSV1) infection usually manifests as gingivostomatitis, pharyngitis, and other cutaneous manifestations. After primary infection, HSV1 enters a latent stage in the neural ganglion cells and is reactivated during physiological stress. Detection of herpesvirus in the lower respiratory tract, including HSV1, cytomegalovirus, Epstein–Barr virus, varicella zoster virus, and human herpesvirus 7, has been reported in severe pneumonia with poor prognosis.[1–4] In critically ill patients with positive herpesvirus from respiratory samples, the presence of pathogenic microorganisms like *Pneumocystis jirovecii* and *Pseudomonas* species has been noted.[5,6] However, HSV1 pneumonia or viral pneumonitis is uncommon and difficult to diagnose, and is often considered an innocent bystander rather than true infection.[1,2] The decision to treat with acyclovir (ACV) or not is a challenge due to there being no current convincing evidence and its association with side effects,[2,7] but in some circumstances antiviral therapy can be beneficial.[8] We describe a patient with severe pneumonia. HSV inclusion bodies on sputum cytology was found accidentally, and the sputum PCR showed positive HSV1 infection. His condition improved without antiviral therapy, though he later died of another bacterial infection.

Case Report

An 80-year-old man with hypertension and dementia presented with fever for 1 day. He also had a productive cough and was brought to the emergency room for dyspnea. The chest X-ray showed mixed interstitial and alveolar infiltration over bilateral lung fields. An influenza A rapid antigen test was positive. Peramivir and empirical piperacillin–tazobactam were prescribed. Further blood culture showed growth of *Enterococcus faecalis* and *Candida glabrata*, so micafungin was added. Abdominal CT was arranged for an intra-abdominal infection survey, but showed no abscess. Transthoracic echocardiography was performed for consideration of infective endocarditis, but showed no vegetation. Subsequent

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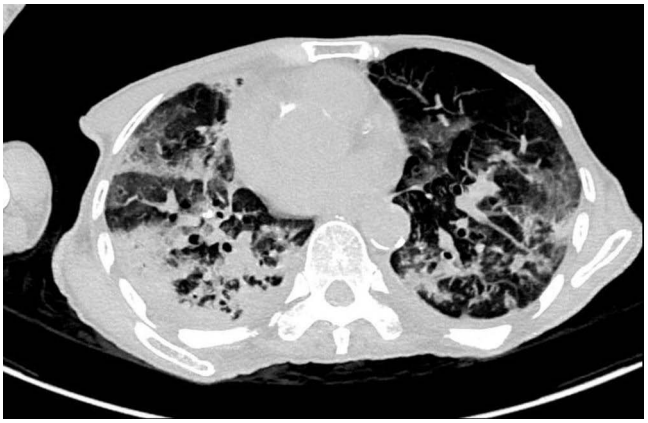

Figure 1 Pneumonia patches on chest CT.

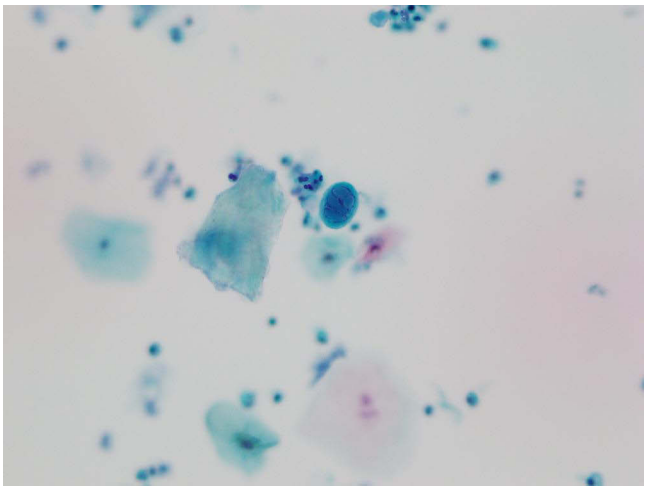

Figure 2 Multinucleated cells with ground-glass appearance on sputum cytology.

blood culture for follow-up showed eradicated bacteria. The piperacillin–tazobactam was shifted to flomoxef for drug-resistant *Klebsiella pneumoniae* from sputum later.

Due to limited improvement in oxygen demand and infiltration persisting on chest X-ray, chest CT was arranged for a tumor survey 8 days after admission and showed pneumonia patches (Figure 1). Sputum cytology was checked and showed no evidence of malignancy, but multinucleated cells with ground-glass appearance (Figure 2) on day 12, characteristic of herpes simplex virus infection. Further PCR showed positive HSV1, but his condition improved gradually later. Chest X-ray showed regression of pneumonia (Figure 3), and the oxygen therapy was tapered from a venturi mask to nasal cannula. ACV was not given.

However, septic shock with desaturation occurred on day 19. Endotracheal intubation was performed, and fluid therapy with norepinephrine was given. Antibiotics were escalated to empirical doripenem and ACV was added. Sputum PCR and culture later revealed *Pseudomonas aeruginosa* infection. In the intensive care unit, the hemodynamics were still unstable with high-dose vasopressor use. Due to his age, the family decided on hospice care. The patient expired 20 days after admission (Figure 4).

Discussion

HSV1 is transmitted by contact with herpetic lesions or secretions. After attaching to the epithelial cells, the virus then enters the sensory nerve endings and develops lifelong latency in our dorsal root ganglion.[9] Viral reactivation during

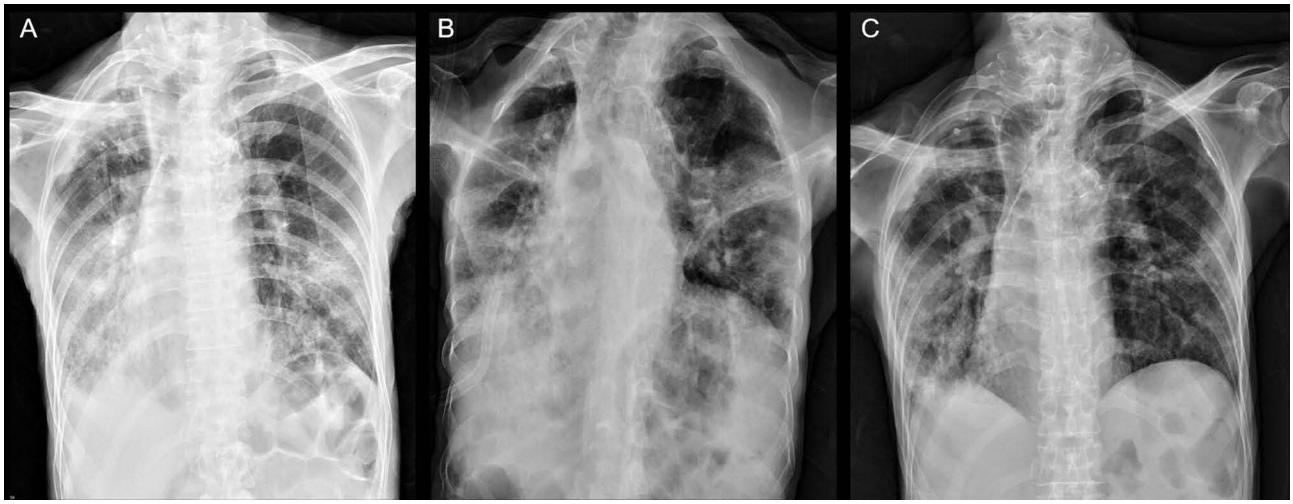

Figure 3 Regression of pneumonia on chest X-ray: **A** day 1, **B** day 7, **C** day 12.

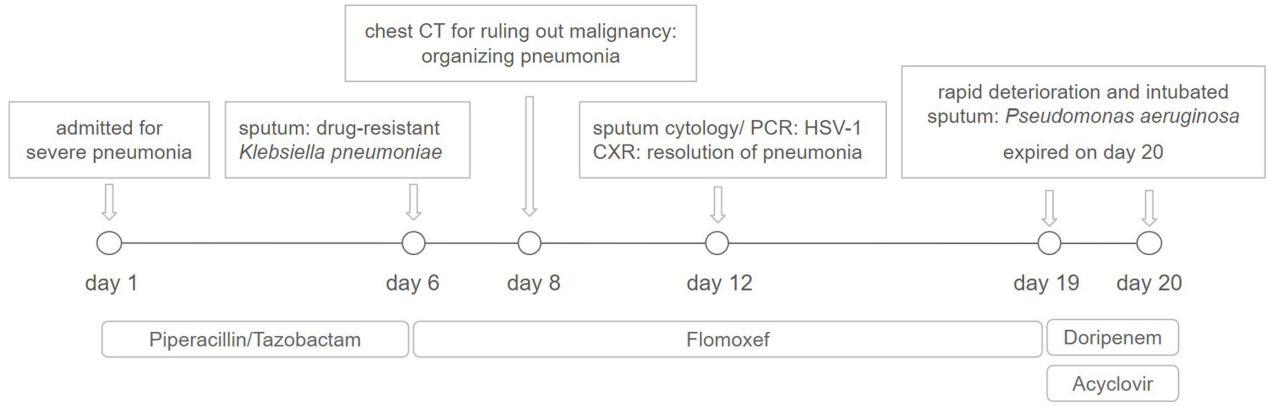

Figure 4 Timeline of clinical course.

stress is reported in critically ill patients.[2,10] Isolation of herpesvirus from respiratory specimens is associated with increased morbidity and mortality.[3,11,12] Reactivation of herpesvirus is also thought to be related with changes in the lower respiratory microbiome. Emergence of pathogenic microorganisms like *Pneumocystis jirovecii, Pseudomonas* spp., and *Burkholderia cepacia* has been reported.[5,6]

HSV1 has been proposed to reach the lower respiratory tract and cause pneumonia by aspiration of salivary secretions or shedding from the oropharyngeal lesions, but true infection or colonization is difficult to distinguish. There is no current gold standard for the diagnosis of HSV1 pneumonia. Clinical criteria and radiological features are similar to general infection and lack specificity. Serological tests provide little information about primary, recurrent, or previous HSV1 infection.[13,14] Detection of HSV1 via PCR from sputum cannot differentiate upper from lower respiratory tract origin, while specimens are more reliable from BAL or bronchial washings. An HSV1 viral load from BAL $>10^5$ copies/mL is associated with worse outcomes, which might provide a diagnostic clue for clinicians.[12] Cytohistological examination for HSV-infected cells with ground-glass inclusion bodies is valuable, but can only be found in a minority of cases.[15,16]

Administration of ACV in patients with positive HSV1 from BAL may improve clinical outcomes, especially those with viral loads $>10^5$ copies/mL;[8,17] however, ACV can lead to renal failure and neurotoxicity in critically ill patients.[10] As such, clarifying infection with colonization and weighing up pros with cons are important. Evidence for ACV therapy dosage and duration of HSV1 pneumonia is not well established. Similar dosing to HSV encephalitis intravenously

10 mg/kg every 8 hours for 10–21 days may be considered.[2] The benefit of corticosteroids is controversial, and routine use of steroids is not recommended.[2,18,19]

In our case, despite positive HSV cytology and PCR results from the sputum, an antiviral agent was not administered initially due to the patient's clinical improvement. Colonization and contamination from the upper respiratory tract were considered, especially in the absence of BAL samples. Additionally, viral load was unavailable in this case. Another possibility is that the patient had a mild HSV1 infection that progressed to severe pneumonia later in combination with bacterial infection. This could account for his eventual serious deterioration, since the average incubation period for HSV is around 1 week.[20]

Conclusion

HSV1 pneumonia presents significant diagnostic challenges, particularly in critically ill patients, in whom clinical and radiological signs often overlap with other infectious etiologies. This case underscores the need for careful interpretation of HSV PCR results and consideration of the clinical context before initiating antiviral therapy. Although HSV1 may contribute to respiratory illness, distinguishing true infection from colonization remains a challenge due to the lack of definitive diagnostic criteria. This case also points to the importance of multidisciplinary management in complex cases involving multiple pathogens, as timely intervention and appropriate antibiotic selection are crucial for patient outcomes. Further studies are warranted to establish clearer guidelines for the management of HSV1 pneumonia, especially regarding the role of antiviral therapy and the implications of viral load in clinical decision-making.

Abbreviations

HSV1, herpes simplex virus type 1; PCR, polymerase chain reaction; CT, computed tomography; ACV, acyclovir; BAL, bronchoalveolar lavage.

Ethics Approval and Informed Consent

Ethics approval was not required by the local ethics committee, as this is a case report with anonymized details.

Consent Statement

Informed consent was obtained from the patient's family due to the patient's inability to provide consent directly. The patient was unable to provide consent because of his dementia, severe medical condition, and eventual death. The family was informed about the nature of the case report, its purposes, and the potential benefits and risks of publication. They provided their consent, understanding all the information provided.

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, interpretation, or in all these areas, took part in drafting, revising, or critically reviewing the article, gave final approval to the version to be published, have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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