AGMR
Annals of Geriatric Medicine and Research

Case Report
pISSN 2508-4798 eISSN 2508-4909
Ann Geriatr Med Res 2022;26(4):367-371
https://doi.org/10.4235/agmr.22.0101

Herpes Simplex Virus Type 1 with Concomitant Pneumonia and Urinary Tract Infection in an Older Patient: A Case Report

Soo Kyun Jung[1], Woo Jung Sung[2], Eun Jin Kim[1]

[1]Department of Internal Medicine, Daegu Catholic University Medical Center, Daegu Catholic University School of Medicine, Daegu, Korea
[2]Department of Pathology, Daegu Catholic University Medical Center, Daegu Catholic University School of Medicine, Daegu, Korea

Corresponding Author:
Eun Jin Kim, MD, PhD
Department of Internal Medicine, Daegu Catholic University School of Medicine, 33, Duryugongwon-ro 17gil, Namgu, Daegu 42472, Korea
E-mail: ejkim77@cu.ac.kr
ORCID:
https://orcid.org/0000-0001-9791-8077

Received: September 18, 2022
Revised: October 18, 2022
Accepted: October 19, 2022

A 76-year-old female patient was unable to ambulate due to sequelae of cerebrovascular disease and had been living in a healthcare facility. On admission, the patient was diagnosed with sepsis and a urinary tract infection caused by *Candida tropicalis*. Chest radiography showed right lung atelectasis, while bronchoscopy showed bronchial stenosis with anthracotic pigmentation in both bronchi. Bronchial washing cytology revealed herpes simplex virus (HSV) type 1-infected cells with intranuclear inclusions and multinucleation on the 7th day. Moreover, the patient showed microscopic hematuria. Urine cytology also revealed HSV type 1-infected cells. The patient was treated with antiviral (acyclovir), antifungal, and antibiotic agents. One week later, follow-up urine cytology revealed the absence of HSV infection, and her condition was stabilized. However, her clinical condition deteriorated due to an infection caused by multidrug-resistant bacterial pathogens, and she eventually died 4 weeks after admission. We describe a case of HSV type 1 pneumonia and urinary tract infection in an older adult patient.

Key Words: Herpes simplex virus, Pneumonia, Urinary tract infections

INTRODUCTION

Herpes simplex virus (HSV) causes a variety of infections that involve mucocutaneous surfaces, the central nervous system, and, occasionally, the visceral organs.[1)] The virus has been associated with pulmonary disease and was first reported by Morgan and Finland.[2)] HSV pneumonia has mostly been reported in immunocompromised hosts and rarely occurs in immunocompetent hosts. Several cases of HSV pneumonia have been reported in Korea. One case was reported in an immunocompromised patient.[3)] Another two cases were reported in older immunocompetent hosts.[4)] Additionally, a case of HSV-induced urethritis was reported in a Korean soldier.[5)]

These reported cases of HSV infection affected several organs. However, no previous reports have described the simultaneous occurrence of a urinary tract infection and pneumonia caused by HSV.

Therefore, we report a cytologically proven case of concomitant HSV pneumonia and urinary tract infection in an older adult female patient with poor performance status.

CASE REPORT

A 76-year-old woman was transferred to Daegu Catholic University Medical Center due to worsening dyspnea. She had been living in a long-term healthcare facility because of an inability to ambulate effectively as a sequela of cerebrovascular disease since 1 year.

She was suffering from hypertension for 18 years, type 2 diabetes mellitus, subarachnoid hemorrhage 17 years ago, endobronchial tuberculosis 14 years ago, and intracerebral hemorrhage 4 years ago. In the last 4 years, she had experienced and then recovered from several episodes of pneumonia.

Her initial vital signs were as follows: blood pressure, 140/54 mmHg; pulse rate, 90 beats/min; body temperature, 36.1°C; and

respiratory rate, 14 breaths/min. Crackle breathing sounds were observed in both the lung fields. She did not show any skin lesions and had an indwelling urinary catheter.

The laboratory test results were as follows: white blood cell count, 361,000/μL (neutrophils 95.8%, lymphocytes 1.1%, and monocytes 2.5%); hemoglobin level, 7.2 g/dL; platelet count 76×10^3/μL; C-reactive protein level, 41.7 mg/L; blood urea nitrogen, 61 mg/dL; creatinine, 0.8 mg/dL; Na, 130 mEq/L; total protein 3.4 g/dL; albumin, 2.2 g/dL; and pro B-natriuretic peptide, 3,669 pg/mL. Arterial blood gas analysis showed a pH level of 7.3999, an arterial carbon dioxide partial pressure of 53.1 mmHg, an arterial oxygen partial pressure of 61.9 mmHg, and a peripheral oxygen saturation of 99% under a fractional inspired oxygen (FiO_2) of 60%.

Initially, *Candida tropicalis* was detected in the blood and urine cultures, while *Klebsiella pneumoniae* (carbapenem-resistant *Enterobacteriaceae*) was detected in the sputum culture.

Chest radiography revealed diffusely increased opacity in the right hemithorax, with right upper lobe atelectasis and collapse consolidation (Fig. 1A). Chest computed tomography (CT) revealed consolidation in the right lung and combined atelectasis with obliteration in the right main bronchi. Chest CT also showed a small consolidation in the left upper lobe (Fig. 1B, 1C).

Based on the above results, the patient was diagnosed with pneumonia, acute respiratory failure, and candidemia. She was treated with meropenem, colistimethate sodium, and fluconazole. Then, high-flow nasal cannula oxygen therapy was administered.

On the second day of admission, flexible bronchoscopy performed in the intensive care unit (ICU) revealed a narrowing of the right main bronchus with anthracotic pigmentation (Fig. 2A, 2B). Bronchial washing for routine culture, acid-fast bacilli staining, *Mycobacterium tuberculosis* polymerase chain reaction (PCR), and cytology were performed on the right main bronchus. No infected cells were observed in bronchial washing cytology. Nine hours after the bronchoscopy, the patient experienced worsening hypoxia and dyspnea despite increasing FiO_2; therefore, endotracheal intubation and mechanical ventilation were performed.

On the 3rd day of admission, urinalysis showed microscopic hematuria; therefore, a urine cytology test was performed. Simultaneously, HSV serology showed that immunoglobulin M (IgM) was negative, and IgG was positive, and the titers were 27.9 index value (negative < 0.9).

On the 7th day of admission, due to weaning failure, percutaneous dilatational tracheostomy with bronchoscopy and repeat bronchial washing cytology in the narrowed and anthracotic right main bronchus were performed bronchial washing cytology revealed HSV type 1-positive cells with intranuclear inclusions and multinucleation (Fig. 3A. 3B) by reverse transcription (RT)-PCR. HSV

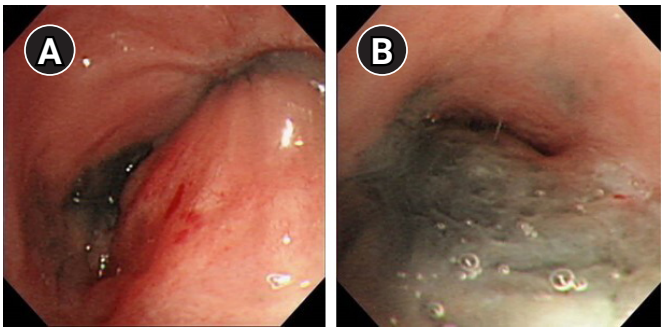

Fig. 2. Bronchoscopy showing narrowing of the right main bronchus with anthracotic pigmentation. (A) Right main bronchus stenosis at the carinal level. (B) Right upper lobe atelectasis with anthracotic pigmentation at the right main bronchus.

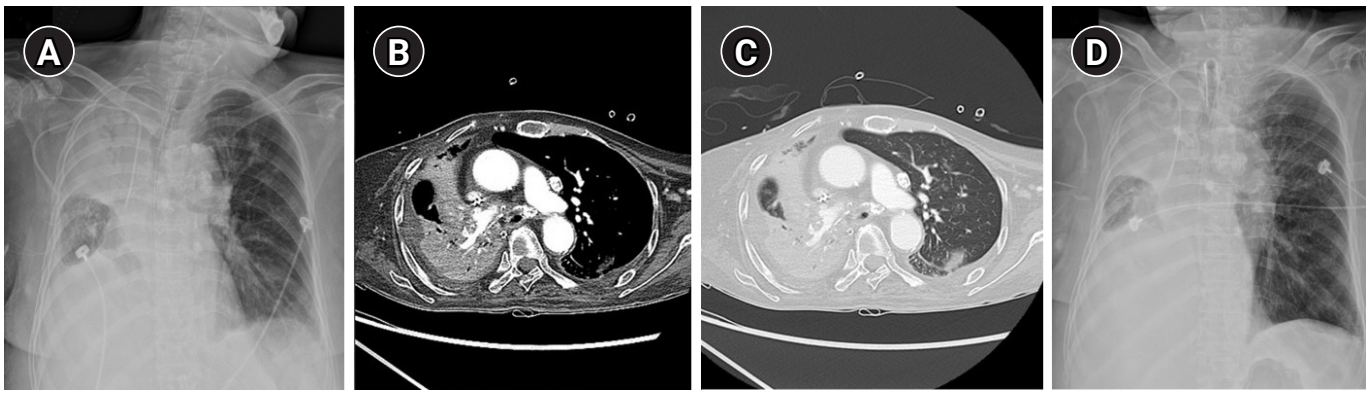

Fig. 1. (A) Chest radiography on admission showing diffuse increased opacity in the right hemithorax with right upper lobe atelectasis and collapse consolidation. (B, C) Chest computed tomography on admission showing consolidation in the right lung and combined atelectasis with obliteration in the right main bronchi. Small consolidation is also visible in the left upper lobe. (D) Chest radiography showing no change in the atelectasis of the right upper lobe after acyclovir treatment.

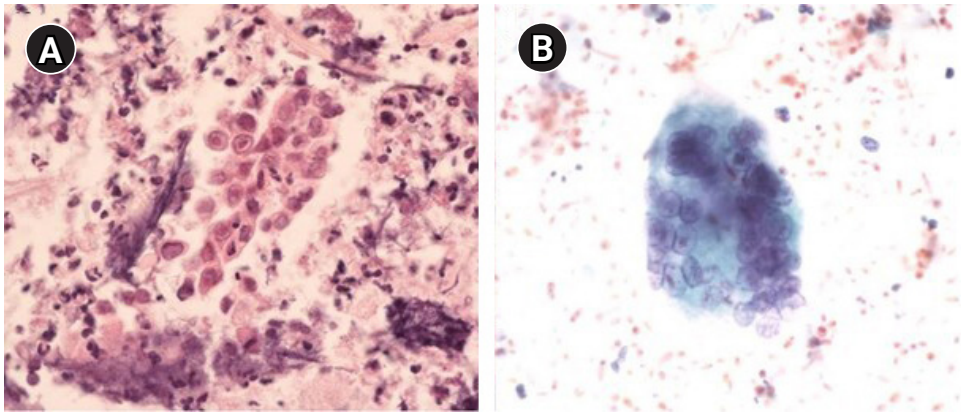

Fig. 3. Bronchial washing cytology showing intranuclear inclusion and multinucleation, suggesting herpes simplex virus-infected cells (Papanicolaou stain, × 400).

type 1-infected cells were also identified by urine cytology performed on the 3rd day of admission. Hence, treatment with 300 mg of acyclovir was initiated three times a day. One week after acyclovir treatment, subsequent urine cytology revealed an absence of HSV infection. However, a repeat bronchoscopy to confirm HSV infection in the bronchi was not performed. After acyclovir treatment, the patient's vital signs remained stable without fever. Her laboratory test results were as follows: white blood cell count, 4,400/μL (neutrophils 88.7%, lymphocytes 7.5%, and monocytes 2.4%); hemoglobin level, 8.6 g/dL; platelet count 65×10^3/μL; C-reactive protein level, 78.1 mg/L. Chest radiography showed stable right upper lobe atelectasis after acyclovir treatment without any other progression (Fig. 1D).

On the 20th day of admission, vancomycin-resistant *Enterococci* were detected in the urine and stool cultures. The patient subsequently developed sepsis. Hence, linezolid 600 mg twice daily was added to the initial treatment. Her urine output decreased insidiously, and acute renal failure occurred. The patient refused to undergo hemodialysis and cardiopulmonary resuscitation; therefore, the caregiver did not attempt to resuscitate the patient. The patient eventually died on the 28th day after admission.

DISCUSSION

This was a case of HSV type 1 pneumonia and urinary tract infection in an older patient who received intensive care. The patient had been bedridden for 1 year and received enteral feeding via a nasogastric tube as a sequela of cerebrovascular disease.

In recent years, the incidence of opportunistic infections has increased owing to widespread organ transplantation and immunosuppressant use. The incidence of viral infections has also increased in recent years. Old age can be considered an immunosuppressive state. Aging does not necessarily lead to an inevitable decline in immune function but is a significant contributing factor to the increased risk and severity of infections in older adults.[6]

Cytology can be used as a rapid and simple routine tool to diagnose viral infections.[7] HSV is rarely detected simultaneously in bronchial washing and urine cytology examination. Because HSV inclusion bodies were observed in urine cytology and RT-PCR of urine specimens showed positive HSV type 1, this case is worthwhile to report.

In general, HSV type 2 causes infection in the genital area.[8] Although not as common as HSV type 2, genital infection in HSV type 1 can cause genital ulceration, pelvic lymphadenopathy, and systemic symptoms, such as fever or myalgia. Occasionally, it causes autonomic dysfunction accompanied by urinary retention or constipation.[9] Few reports have described genital infections caused by HSV type 1. A previous report observed perineal skin vesicles and diagnosed the infection by viral culture from the lesion. In another report, a patient was diagnosed with plasma positive for HSV type 1 by PCR; simultaneously, the HSV type 1 antibody titers were IgM-negative and IgG-positive, as observed in the present case.[9] However, no previous reports have described HSV infection in urine cytology due to HSV type 1, although a case of HSV type 2, confirmed by bladder biopsy due to hemorrhagic cystitis, has been reported. In the present case, the cytological examination was performed because of hematuria and revealed HSV type 1; therefore, hematuria may be an important symptom of HSV infection.[10]

In HSV pneumonia, focal disease may start as an oropharyngeal disease and spread to the lower respiratory tract, whereas diffuse pneumonia is associated with hematogenous dissemination of the virus from mucocutaneous oral or genital lesions into the lungs.[11] HSV type 1 may reach the lower respiratory tract through three

different mechanisms. First, contiguous spread to the lung parenchyma or aspiration of the virus in patients shedding the virus from mucocutaneous or oropharyngeal lesions.[12] Second, hematogenous seeding, as supported by Ramsey et al.[11] The recovery of HSV from circulating lymphocytes or peripheral buffy coat blood cells supports this mechanism.[13] Third, reactivation of latent infection within the vagal ganglion, which spreads along the vagus nerve to the lung epithelium, has also been postulated.[14] HSV pneumonia can be provoked by aspiration of infected exudates from the upper airways.[15] Simoons-Smit et al.[1] noted the presence of HSV in the upper and lower respiratory tracts in 22% and 39% of ICU patients, respectively. Critically ill patients in the ICU ventilated for > 5 days showed an increased risk of herpes bronchopneumonia; these patients also had worse outcomes.[16]

Distinguishing between HSV colonization and pneumonitis is difficult. This case did not show a typical viral pneumonia pattern, such as ground-glass opacities, because it was difficult to observe this pattern due to physical stenosis of the right upper lobe atelectasis that might be caused by anthracofibrosis. Cytological confirmation of HSV type 1 in bronchoalveolar washing fluid, but not in tracheal or oral aspiration samples, suggests a true infection.[16] The improvement in leukocytosis, inflammatory markers, and vital signs after treatment with acyclovir also suggested a true infection, although other factors may also have played a role as an ICU patient.

In the present case, we performed real-time HSV PCR to confirm the diagnosis. A complete diagnosis of HSV is difficult to establish because the clinical criteria, radiological features, and laboratory findings lack specificity. In patients with suspected HSV infection, HSV PCR and culture are the most commonly used tests to confirm the diagnosis. In addition to PCR and culture, other types of tests include direct fluorescent antibody and serological assays. However, these methods are not recommended owing to their poor sensitivity compared with that of PCR and culture. Serological tests cannot differentiate between primary, recurrent, and previous HSV infections. The specificity of both cytological examination and virus culture increases when the samples are collected by bronchoalveolar lavage.[17]

HSV pneumonia is associated with increased mortality rates in critically ill patients.[18] Clinical studies on HSV respiratory infections in critically ill patients have reported up to 63% mortality.[1] One study reported a slow decline in HSV viral loads after the initiation of HSV treatment with acyclovir, with no deaths among the treated patients. However, the mortality rate was not significantly higher in patients who did not receive acyclovir. Similarly, Schuller et al.[19] reported no differences in mortality, duration of mechanical ventilation, or length of stay between patients with and without acyclovir administration.[1] However, a recent study demonstrated that acyclovir treatment was associated with a significantly longer time to death in the ICU, reduced hazard ratio for ICU death, and clinically improved circulatory and pulmonary oxygenation functions in patients with ventilator-associated pneumonia, antibiotic treatment failure, and high levels of HSV replication.[20] The patient in the present case was bedridden and infected with multidrug-resistant organisms as well as HSV, and eventually died of complications from HSV infection, multidrug-resistant bacterial infection, and consequent treatment.

In conclusion, older age with poor general condition can lead to opportunistic infections, similar to immunocompromised hosts. Therefore, cytology may be useful for the diagnosis of viral diseases. In addition, this study is crucial as it reports a rare case of HSV infection, especially HSV type 1, found simultaneously in the urine and bronchial washing fluid.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization: SKJ, WJS; Data curation: EJK; Investigation: SKJ, WJS; Methodology: WJS; Project administration: WJS, EJK;Supervision: EJK; Writing-original draft: SKJ; Writing-review & editing: SKJ, WJS, EJK.

REFERENCES

1. Simoons-Smit AM, Kraan EM, Beishuizen A, Strack van Schijndel RJ, Vandenbroucke-Grauls CM. Herpes simplex virus type 1 and respiratory disease in critically-ill patients: real pathogen or innocent bystander? Clin Microbiol Infect 2006;12:1050-9.
2. Morgan HR, Finland M. Isolation of herpes virus from a case of atypical pneumonia and erythema multiforme exudativum with studies of four additional cases. Am J Med Sci 1949;217:92-5.
3. Kim JK, Lee CH, Kang KW, Seo GY, Chung MP, Kim H, et al. Herpes simplex virus pneumonia in immunocopmromised host. Tuberc Respir Dis 1999;46:82-8.
4. Kim DS, Kim SJ, Lee YW, Hong SR, Ko IH. A case report of tracheobronchitis by herpes simplex virus, type I. Korean J Intern Med 1986;1:249-53.
5. Kim HJ, Park JK, Park SC, Kim YG, Choi H, Ko JI, et al. The

prevalence of causative organisms of community-acquired urethritis in an age group at high risk for sexually transmitted infections in Korean Soldiers. J R Army Med Corps 2017;163:20-22.
6. Dewan SK, Zheng SB, Xia SJ, Bill K. Senescent remodeling of the immune system and its contribution to the predisposition of the elderly to infections. Chin Med J (Engl) 2012;125:3325-31.
7. Braz-Silva PH, Magalhaes MH, Hofman V, Ortega KL, Ilie MI, Odin G, et al. Usefulness of oral cytopathology in the diagnosis of infectious diseases. Cytopathology 2010;21:285-99.
8. Benedetti J, Corey L, Ashley R. Recurrence rates in genital herpes after symptomatic first-episode infection. Ann Intern Med 1994;121:847-54.
9. Mancino P, Dalessandro M, Falasca K, Ucciferri C, Pizzigallo E, Vecchiet J. Acute urinary retention due to HSV-1: a case report. Infez Med 2009;17:38-40.
10. LeBlanc RE, Maleki Z. Herpes simplex viral cytopathic effect in urine cytology. Diagn Cytopathol 2013;41:61-2.
11. Ramsey PG, Fife KH, Hackman RC, Meyers JD, Corey L. Herpes simplex virus pneumonia: clinical, virologic, and pathologic features in 20 patients. Ann Intern Med 1982;97:813-20.
12. Nash G. Necrotizing tracheobronchitis and bronchopneumonia consistent with herpetic infection. Hum Pathol 1972;3:283-91.
13. Graham BS, Snell JD. Herpes simplex virus infection of the adult lower respiratory tract. Medicine (Baltimore) 1983;62:384-93.
14. Tuxen DV, Cade JF, McDonald MI, Buchanan MR, Clark RJ, Pain MC. Herpes simplex virus from the lower respiratory tract in adult respiratory distress syndrome. Am Rev Respir Dis 1982;126:416-9.
15. Odani K, Tachibana M, Tamashima R, Tsutsumi Y. Herpes simplex virus pneumonia: importance of aspiration etiology. Case Rep Pathol 2019;2019:7623576.
16. Luyt CE, Combes A, Deback C, Aubriot-Lorton MH, Nieszkowska A, Trouillet JL, et al. Herpes simplex virus lung infection in patients undergoing prolonged mechanical ventilation. Am J Respir Crit Care Med 2007;175:935-42.
17. Luginbuehl M, Imhof A, Klarer A. Herpes simplex type 1 pneumonitis and acute respiratory distress syndrome in a patient with chronic lymphatic leukemia: a case report. J Med Case Rep 2017;11:329.
18. Engelmann I, Gottlieb J, Meier A, Sohr D, Ruhparwar A, Henke-Gendo C, et al. Clinical relevance of and risk factors for HSV-related tracheobronchitis or pneumonia: results of an outbreak investigation. Crit Care 2007;11:R119.
19. Schuller D, Spessert C, Fraser VJ, Goodenberger DM. Herpes simplex virus from respiratory tract secretions: epidemiology, clinical characteristics, and outcome in immunocompromised and nonimmunocompromised hosts. The Am J Med 1993;94:29-33.
20. Schuierer L, Gebhard M, Ruf HG, Jaschinski U, Berghaus TM, Wittmann M, et al. Impact of acyclovir use on survival of patients with ventilator-associated pneumonia and high load herpes simplex virus replication. Crit Care 2020;24:12.