



# An unusual case of herpes simplex virus pneumonia with cavitory and necrotic changes

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## ABSTRACT

Ground glass opacities, consolidation, and pleural effusions are observed in herpes simplex virus (HSV) pneumonia. Neither necrosis nor cavitation has been reported in areas of parenchymal disease. We describe a case of HSV pneumonia with unusual multiple cavitory and necrotic changes in an immunocompetent person. To our knowledge, this is the first reported case of HSV pneumonia with multiple cavitory and necrotic changes in areas of consolidation and nodules.

## 1. Introduction

Herpes simplex virus (HSV) pneumonia develops most frequently in patients with an airway injury or immunosuppression. Most affected patients present with a combination of ground glass opacity (GGO) and consolidation [1]. Thus, a characteristic radiographical pattern for HSV pneumonia has not yet been identified [2]. The specific pathological findings for a definite diagnosis include the presence of intranuclear inclusion bodies on hematoxylin and eosin (H&E) staining or a positive immunohistochemical (IHC) staining result [3].

We describe a case of HSV pneumonia in an immunocompetent patient without the involvement of any risk factors. The patient initially presented with multiple areas of consolidation and nodules in both lungs that eventually progressed to unusual multiple cavitory and necrotic changes. HSV pneumonia was confirmed by both intranuclear inclusion bodies and positive IHC staining. Intravenous acyclovir therapy was effective for improving the patient's chest radiographic findings and alleviating respiratory failure.

## 2. Case report

A 63-year-old woman was referred on January 15, 2019. She was a social worker and a non-smoker. The patient had been treated for community-acquired pneumonia for 15 days at the previous hospital until her condition deteriorated to respiratory failure. On January 2, a

chest computed tomography (CT) scan showed patchy consolidations and small nodules in both lungs (Fig. 1). She was intubated on January 4.

Upon admission to the intensive care unit (ICU) for mechanical ventilation, the vital signs were stable. Laboratory tests revealed a white blood cell count of 13,470/mm<sup>3</sup>, albumin 1.9 g/dL and sodium 152 mEq/L. She had a medical history of hypertension. Broad spectrum antibiotics were administered, but the patient did not improve. On hospital day (HD) 9, a chest CT scan showed progressive necrotic and cavitory changes in areas with multifocal consolidations and multiple small nodules in both lungs (Fig. 2). Abundant bilateral pleural effusions were observed with multiple necrotic lymph nodes. A portable bronchoscopy (FOB) (Olympus MAF-TM) was performed in the ICU on the same day. The FOB showed an erythematous, friable mucosa with scattered whitish plaque-like lesions especially on both lower lobe bronchi (Fig. 3). A biopsy showed ulceration, necrotic inflammatory exudates, extensive squamous metaplasia and several multinucleated epithelial cells containing intranuclear inclusions in the exudate on H&E staining, consistent with HSV or varicella-zoster virus: IHC staining showed a positive reaction to HSV (Fig. 4) and a negative reaction to Cytomegalovirus. Negative results were also obtained for acid-fast bacilli, Gomori's methenamine-silver, and periodic acid-Schiff staining tests. Viral serology; PCR; and viral, bacterial, and fungal cultures with bronchial aspirate showed negative results. Autoantibody testing such as anti-neutrophil cytoplasmic antibodies, antinuclear antibody

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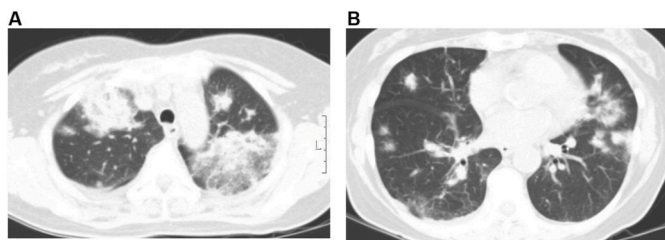
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**Fig. 1.** Chest CT scan on January 2. Peribronchial, subpleural patchy consolidations with an air bronchogram and multiple small nodules in both lungs. Small bilateral pleural effusions and multiple lymphadenopathies in both hilar, right lobar, right and left interlobar areas were also noted.

and rheumatoid factor for vasculitis screening were all negative.

Acyclovir therapy was started on HD 10 whilst all other antibiotics were discontinued. Percutaneous catheter drainage was performed for left pleural effusion which was removed 5 days later. Pleural fluid was exudative with a polymorphonuclear leukocyte predominance of 84%. The patient improved gradually; she was moved to the general ward after being weaned off mechanical ventilation on HD 31.

A newly developed consolidative lesion of the right lower lobe (RLL) was first noted on HD 41 that had deteriorated further when observed on HD 53. A chest CT scan performed on HD 53 showed an overall improvement, but a necrotic nodule was seen on the RLL. Another CT scan on HD 78 showed further improvement of the multiple necrotic or cavitory lesions and bilateral pleural effusions. However, there was no change in the RLL nodule. Percutaneous needle biopsy (PCNB) was performed on HD 80, which showed no viral cytopathic cells. IHC staining was negative for HSV. Acyclovir therapy was continued for 12 weeks and the condition of the RLL nodule subsequently improved (Fig. 5). The patient was discharged on HD 104. On her follow-up visit after 2 weeks, the chest X-ray showed no active lesions.

### 3. Discussion

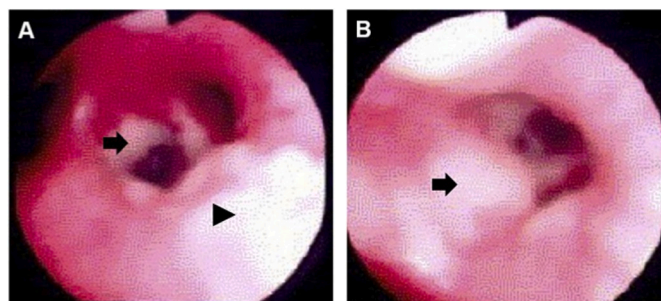
HSV pneumonia is uncommon and well tolerated in healthy individuals; however, it is often observed in immunocompromised patients or individuals whose airways have been traumatized by intubation, smoke inhalation, or cigarette smoking [4]. This case is reported in an immunocompetent patient who did not present with any risk factor. The patient was intubated during the course of pneumonia.

According to CT scan findings for 8 patients with HSV type 1 pneumonia, all patients had multifocal areas of GGO, 6 of whom had areas of air-space consolidation, and 4 among them also had reticular opacities. One patient had multiple small pulmonary nodules. Small pleural effusions were present in 7 patients. Adenopathy was present in one patient, and two additional patients had multiple small mediastinal nodes [1]. In 3 patients with HSV type 2 pneumonia, two had irregular and multiple large nodules, ranging from 10 to 20 mm in diameter and were distributed randomly throughout the lungs [5]. In this case, although the

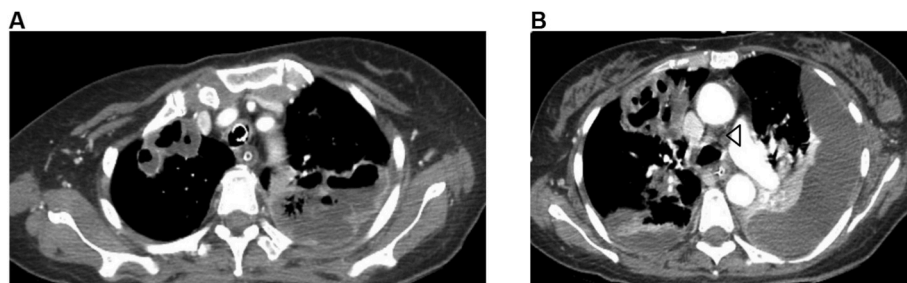
organism was not subtyped, an initial chest CT scan showed multifocal consolidations and nodules with lymphadenopathies and bilateral pleural effusions. GGO and reticular opacity were not seen.

A follow-up chest CT scan showed unusual necrotic and cavitory changes in multifocal areas of consolidation and nodules, along with necrotic changes in the lymph nodes. Cavitation during the course of a disease has been shown to occur only in viral pneumonia caused by the H5N1 avian influenza [6]. In HSV pneumonia, neither necrosis nor cavitation has been reported in areas of parenchymal disease [1]. In a small study ( $n = 78$ ) of immunocompromised patients with lung infections, the presence of a cavity on CT scan of the lungs essentially ruled out a viral infection; however, the etiologies of the cavities among these patients were equally divided among bacterial, mycobacterial, and fungal infections [7].

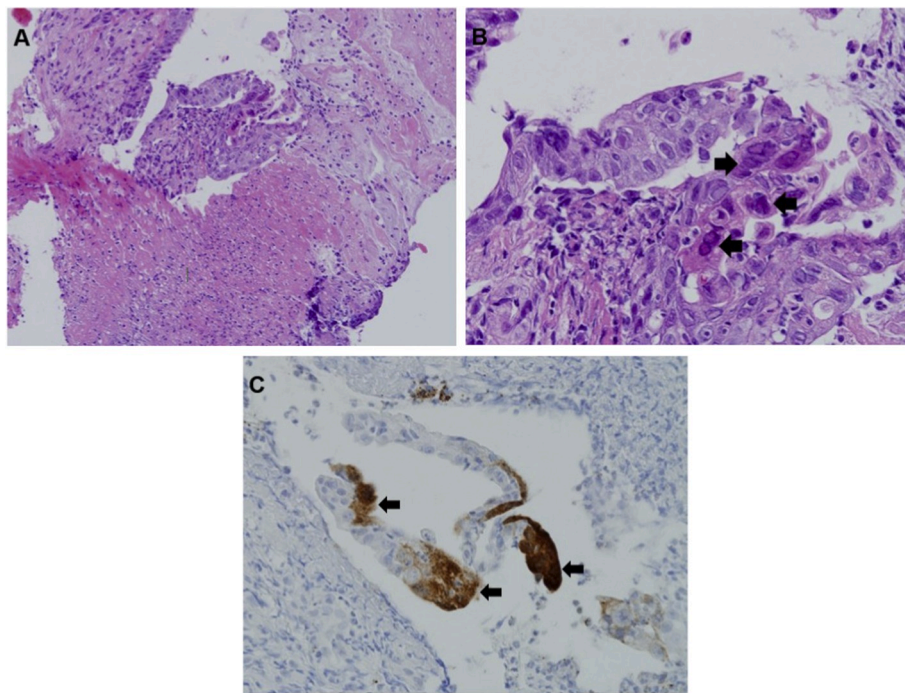
The diagnosis of HSV pneumonia in immunocompromised hosts, as well as in immunocompetent patients, is difficult because the clinical criteria, laboratory findings and radiological features lack specificity. Histologically, diagnosis depends on recognition of HSV cytopathic changes in infected cells such as multinucleation, nuclear ground-glass opacities and intranuclear inclusion, collectively [2]. The viral cytopathic effect is important to determine the presence of HSV as a marker of the underlying disease severity (innocent bystander) as opposed to a true pathogenic organism [3]. Evidence of a viral cytopathic effect in cytologic and/or histopathologic specimens with the confirmation of the HSV infection via cultures, PCR, or immunohistochemical staining is required [8]. In this case, the FOB findings were similar to those reported previously as confirmed by the presence of white plaque-like lesions within the bronchi and mucosal erythema and edema [1,2] but there was no purulent secretion. Endobronchial biopsies done in both lower lobe bronchi revealed a Cowdry type B inclusion body and a positive IHC staining for HSV, thus confirming an active HSV infection. HSV inclusion bodies can be of 2 types, Cowdry A and B [9,10], and in this case, Cowdry B bodies were seen. We would have wanted to obtain a biopsy of the peripheral cavitory and necrotic lung lesions, but neither a transbronchial lung biopsy nor a PCNB was possible because the patient



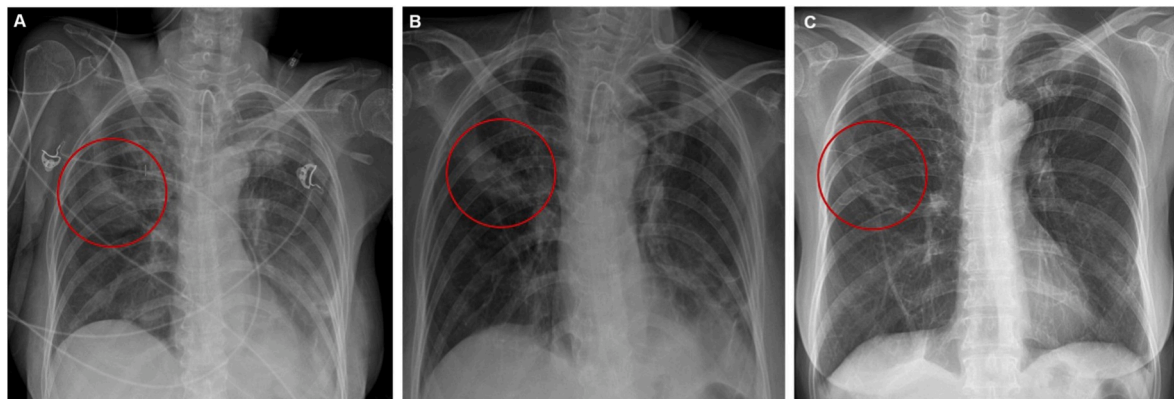
**Fig. 3.** Bronchoscopic findings. The FOB showed scattered whitish plaque-like lesions, especially on the distal right intermediate bronchus (arrowhead) and right lower lobe bronchus (arrow) (A) and left lower lobe bronchus (arrow) (B).



**Fig. 2.** Chest CT scan on January 23. Progressed necrotic and cavitory changes of the multifocal consolidation and multiple small nodules in both lungs. Abundant bilateral pleural effusions were observed. Multiple lymphadenopathies also showed necrotic changes (arrowhead).



**Fig. 4. Pathologic findings of the bronchoscopic biopsies** (A) The bronchial wall showed extensive necrosis with acute inflammation. The remaining bronchial epithelial cells showed squamous metaplasia (x200). (B) There were multinucleated epithelial cells containing dense, ground glass intranuclear inclusions surrounded by a basophilic rim (Cowdry type B) (arrows) (x600). (C) IHC staining with the HSV confirmed the presence of viral cytopathic cells (arrows) (x600).



**Fig. 5. Chest X-rays for RLL necrotic nodule.** An RLL necrotic nodule (circles) developed on HD 41 (A), and deteriorated on HD 53 (B). The nodule finally improved on HD 103 (C).

was on mechanical ventilation.

We used acyclovir at a dose of 10 mg/kg *t. i. d.* [11] because of the extensive necrotic and cavitary changes associated with pneumonia including the lymph nodes. The median duration of acyclovir therapy has been reported to be as long as 13 days (range, 5–21 days) for HSV pneumonia in patients with solid tumors [12]. However, we used it for the relatively long period of 12 weeks because the patient showed a slow improvement. A necrotic nodule developed on the RLL after 4 weeks since acyclovir deteriorated about 2 weeks later. We performed a PCNB of the RLL lesion after 10 weeks of the acyclovir treatment to decide whether to continue with acyclovir regimen. The results of these tests confirmed the absence of any cytopathic findings. We terminated the acyclovir therapy after the RLL lesion finally improved.

#### 4. Conclusions

In this case, we confirmed the presence of an HSV pneumonia by

typical endobronchial lesions, histopathological findings, IHC staining, and overall improvement on follow-up chest CT scans with acyclovir therapy. There were no other bacterial pathogens or fungi in the serial cultures and serologic studies. Despite being very unusual, HSV should be considered as a differential diagnosis in cases of extensive parenchymal necrotic and cavitary pneumonia in immunocompetent patients.

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#### Informed consent

Yes.

## Declaration of competing interest

None.

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