Herpes Simplex Virus Bronchopneumonia in a Non-immunocompromized Individual

Akiko Miyazato, Hirotugu Kishimoto*, Kazunori Tamaki*, Ken Nakama** and Atsushi Saito

Abstract

We report a rare case of herpes simplex virus (HSV) bronchopneumonia in an otherwise healthy middle-aged individual. Bronchoscopy indicated scattered white-coated lesions in the bronchial mucosa. The diagnosis was established following immunohistopathological staining for HSV of specimens obtained by bronchial biopsy. This case suggests that HSV could be a pathological agent of not only oral and genital mucosal lesions but also lower respiratory tract infection.

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Key words: bronchoscopy, bronchial ulcerative lesions, necrotic bronchopneumonia, immunohistopathological staining

Introduction

It is known that some species of herpes virus, such as herpes simplex type I and II (HSV-I and -II), herpesvirus 6, herpesvirus 8, varicella-zoster virus (VZV), and cytomegalovirus (CMV) can cause pneumonia. There are many reports of VZV pneumonia in non-immunocompromised patients with chickenpox. In comparison, HSV is known to cause pneumonia only in immunocompromised hosts, such as those with severe burns (1) and neoplasms (2,3), and is strongly associated with acute respiratory distress syndrome (ARDS) (4). Here, we report a rare case of HSV bronchitis and pneumonia in an otherwise a healthy individual.

Case Report

A 49-year-old, previously healthy man visited the local hospital for common cold-like symptoms. The prescribed medications were ineffective and he was referred to our hospital for further management of persistent dry cough and fever, 10 days after the appearance of symptoms. He was a smoker (4-5 cigarettes a day) for 30 years. Physical examination was not remarkable and rales could not be auscultated on chest examination. There were no skin or oral lesions, including vesicles. The chest roentgenogram (Fig. 1A) showed bilateral patchy shadows and chest computer tomography (Fig. 1B) revealed bilateral nonsegmental nodular shadows. Laboratory studies showed leukocytosis (17,200/mm³), an elevated serum level of C-reactive protein (CRP, 13.3 mg/dl) and a high erythrocyte sedimentation rate (ESR, 49 mm/h). The serum level of anti Mycoplasma pneumoniae antibody was negative (Table 1). Because he had no sputum for examination, bronchoscopy and bronchial washing were performed to determine the causative organism(s). Bronchoscopy revealed scattered white-coated lesions in the mucosa extending from the trachea to the bronchi (Fig. 2). However, no pathogens were isolated from the bronchial washing fluid, including bacteria, fungus and mycobacterium. The histopathological findings of white-coated lesions showed erosive area covered with fibrinous exudate and surrounding squamous metaplasia (Fig. 3A). Cytology of transbronchial brushing and washing fluid showed the presence of a small number of cells with ground-glass intranuclear changes. Such histopathological and cytological findings are characteristic of herpes virus infection. Consistent with this provisional diagnosis, herpes virus antigen was detected in epithelial cells of bronchi by using immunohistopathological staining (Fig. 3B). The identified antigen was that of HSV-II. The patient recovered spontaneously without any treatment, and chest roentgenographic findings resolved completely three weeks after his visit to our hospital (Fig. 4). Laboratory findings at that stage showed improvement, including CRP, 0.25 mg/dl, ESR, 1 mm/h and improvement of leukocyte count (10,500/mm³). HSV complement fixation titer at recovery was 1 : 32 (normal level <1 : 4) with a simultaneous varicella complement fixation titer of 1 : 4 (normal level <1 : 4) (Table 1). Repeat bronchoscopy showed improvement of the previously noted lesions.
Herpes Simplex Bronchopneumonia

Figure 1. A posteroanterior chest radiograph showing multilobular patchy and nodular shadows mainly in the right lung field (A). A CT scan demonstrating the presence of nodules surrounding the airways in the bilateral upper lung field (B).

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<th>Table 1. Laboratory Findings</th>
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<th>Microbiological examination</th>
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<td>Bronchial lavage fluid:</td>
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<td>Gaffky, culture of mycobacterium</td>
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Discussion

In 1949, Morgan and Finland (5) reported for the first time the postmortem isolation of herpes virus from the lung of a patient who had died with an atypical pneumonia, indicating that HSV could be a respiratory tract pathogen.

The diagnosis of HSV pneumonia is based on the presence of characteristic cytological and histological changes, such as intranuclear inclusions or homogenization of the nuclear chromatin, in specimens obtained by tracheobronchial brushing or biopsy (3, 6). However, Byers et al (7) indicated that characteristic nuclear changes could not be detected in hematoxylin-eosin stained sections in burns cases, probably because the associated inflammation and necrosis, resulting in pyknotic and apoptotic nuclei, masked intranuclear inclusions. Even in that...
situation, the cytopathic changes seen in lavage fluid or in tracheobronchial secretions are less prone to the problems of identification posed by accompanying inflammation and necrosis (7). To confirm the diagnosis, immunofluorescence or immunohistochemical studies with anti-virus antibodies should be performed, which have high sensitivity and specificity (6, 8). Viral culture is also useful to confirm the diagnosis. However, HSV can be cultured from the oral cavity of 1 to 5% of asymptomatic adults and it is difficult to distinguish between the carrier state and true infection when the virus is cultured from the
sputum (3). Serologic techniques may be helpful in the diagnosis of primary HSV infections when a four-fold rise in titer is observed between acute sera, whereas such rises may or may not be observed in recurrent infections (9). Infection of the lower respiratory tract by HSV almost always represents reactivation of latent virus (10), suggesting serological tests are rarely of value in recurrent infections. However, paired antibody titers may be useful in predicting prognosis. If the titers do not rise in the presence of lower respiratory tract infection caused by HSV, the outcome is more likely to be fatal (3).

HSV is composed of two subtypes, type I (HSV-I) and type II (HSV-II). HSV-I is transmitted primarily by contact with oral secretions and is most commonly associated with oral disease, such as gingivostomatitis in children or recurrent labialis in older individuals. HSV-II is best known as the cause of herpes genitalis, a sexually transmitted disease characterized by ulcers of the vagina, vulva, and perineum in women and glans penis, prepuce, and penis shaft in men. However, HSV-II has also been detected in lesions of 10–20 percent of patients with herpes labialis. Similarly, HSV-I has been detected in 10–30 percent of patients with herpes genitalis (9). Recurrent infection occurs frequently with both HSV-I and HSV-II.

Several mechanisms have been proposed for pathogenic mechanisms of herpes virus infection of the lower respiratory tract. Based on the presence of concomitant oropharyngeal lesions and history of tracheal intubation in many affected patients, aspiration or contiguous spread has classically been considered as the mode of HSV spread to the respiratory tract (11). However, several investigators have found no evidence of oral infection or history of intubation (12), suggesting other mechanisms, such as hematogenous transmission from an extrapulmonary lesion, may be involved in the pathogenesis. It has also been hypothesized that there may be direct tracheobronchial spread of reactivated virus originally present within vagal ganglia (13).

The pathologic features of HSV-I infection of the respiratory tract include focal or diffuse ulcers in the tracheobronchial epithelium with or without necrotizing pneumonia (2), whereas HSV-II infection tends to show interstitial pneumonia and less prominent airway involvement than HSV-I.

Radiological manifestations of HSV pneumonia have been described in few reports. However, Aquino et al (14) reported that HSV-I pneumonia tends to distribute multifocally, subsegmentally and opacities are predominantly of the ground glass attenuation with some areas of consolidation. Occasionally, there are poorly defined nodular opacities, corresponding on high resolution computed tomography (HRCT) to soft tissue nodules (15). In comparison, HSV-II pneumonia tends to show diffuse alveolar damage or interstitial pneumonia. These differences in clinical features between HSV-I and II indicate that HSV-I bronchopneumonia tends to occur through aspiration or direct spread of oral lesions, whereas HSV-II pneumonia is caused by hematogenous dissemination in most cases.

In the present case of bronchopneumonia, which was caused by HSV-II, there were multiple ulcers in the tracheobronchial tree, and CT findings revealed multifoetal nodular shadows continuous with the bronchial branches. Although no oral lesions could be detected in this patient, these features suggest that reactivated HSV-II in the oropharyngeal area was aspirated and caused pneumonia like HSV-1. In another explanation, direct tracheobronchial spread of reactivated virus within vagal ganglia might have occurred.

Graham and Snell (3) reported that the prognosis of HSV pneumonia seems to be largely dependent on the immunologic status of the host and the underlying disease. In the absence of such conditions, HSV infection of the lower respiratory tract is not necessarily a fatal disease. Consistent with that, the present case progressed to HSV bronchopneumonia and recovered spontaneously without treatment.

With respect to treatment, marked improvement with acyclovir has been reported (16), and prophylactic administration of acyclovir seems to prevent the high incidence of HSV in ARDS patients (17). On the other hand, Schuller et al (18) reported the lack of significant difference in mortality between patients treated with acyclovir and untreated patients, and concluded that the availability of treatment with acyclovir is uncertain and controversial at this time. However, patients who are critically ill with lower respiratory tract infection in whom HSV is isolated from the respiratory tract seem to benefit from treatment with acyclovir.

The present case suggests that HSV bronchopneumonia could be erroneously classified as pneumonia caused by unknown pathogen. In such cases, cytological examination of bronchial secretion would be helpful for establishment of the correct diagnosis and washing and biopsy at bronchoscopy is most useful to confirm the diagnosis.
References


