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Herpes simplex virus 1 pneumonia: conventional chest radiograph pattern

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Abstract The aim of this study was to describe the findings on plain chest radiographs in patients with herpes simplex virus pneumonia (HSVP). The study was based on 17 patients who at a retrospective search have been found to have a mono-infection with herpes simplex virus. The diagnosis was established by isolation of the virus from material obtained during fiberoptic bronchoscopy (FOB) which also included broncho-alveolar lavage and tissue sampling. Fourteen patients had a chest radiograph performed within 24 h of the date of the FOB. Two radiographs showed no abnormalities of the lung parenchyma. The radiographs of the other 12 patients showed lung opacification, predominantly lobar or more extensive and always bilateral. Most patients presented with a mixed airspace and interstitial pattern of opacities, but 11 of 14 showed at least an air-space consolidation. Lobar, seg-

mental, or subsegmental atelectasis was present in 7 patients, and unilateral or bilateral pleural effusion in 8 patients, but only in 1 patient was it a large amount. In contradiction to the literature which reports a high correlation between HSVP and acute respiratory distress syndrome (ARDS), 11 of 14 patients did not meet the pathophysiological criteria for ARDS. The radiologist may suggest the diagnosis of HSVP when bilateral airspace consolidation or mixed opacities appear in a susceptible group of patients who are not thought to have ARDS or pulmonary edema. The definite diagnosis of HSV pneumonia can be established only on the basis of culture of material obtained by broncho-alveolar lavage.

Key words Herpes simplex virus · Pneumonia · Chest radiograph · ARDS

Introduction

Herpes simplex virus (HSV) has been isolated from nearly all visceral and mucocutaneous sites. The clinical manifestations and course of HSV infections depend on the anatomic site of the infection, the age and immune status of the host, and the antigenic type of the virus [1]. Herpes simplex virus is a DNA-type virus that belongs to the human herpes virus (HHV) group. The most well-known HHV are HSV types 1 and 2 and HHV type 3 (varicella-zoster virus). HSV 1 and 2 become latent in

trigeminal and lumbosacral dorsal-root ganglia after a primary infection of the oropharynx leading to gingivostomatitis and/or pharyngitis (HSV1) or of the genital region (HSV2) [2].

From autopsy reports dating back to the early 1970s, it is known that herpes simplex virus may cause pneumonia [3, 4]. It was thought that all HSV-related pneumonias were the result of reactivation of the virus due to a diminished immune state or through local airway trauma [5, 6, 7]. Later reports did indeed show an association of HSV infection with an immunosuppressed

state in patients who had had chemotherapy, organ transplantation, or other major surgery, and also in patients infected with human immunodeficiency virus (HIV) or other diseases which decrease immunity [7, 8, 9, 10, 11, 12]. All these conditions were shown to be associated with an increased risk of herpes simplex virus pneumonia (HSVP). It is also known that intubation causes initial upper airway infection perhaps as a result of local trauma which might lead to HSVP. Tuxen et al. reported a relationship between HSVP and the diagnosis of acute respiratory distress syndrome (ARDS) established clinically and radiologically [13, 14, 15]. This was later confirmed in an autopsy report of 54 patients suffering from burns [16]. Hematogenous spread to the lungs from infected lesions may also occur. This could be initiated by disruption of virally infected tissues by burns or smoke inhalation.

In the international literature the chest radiographic findings of HSVP have been rarely reported [5, 6, 17, 18, 19, 20]. The present study was undertaken to (a) document the spectrum of abnormalities on chest radiographs in patients with a proven HSVP, and (b) try to detect if there was any pattern which might lead to a better recognition of this fairly unknown disease.

While we were collecting our data Aquino et al. published a study on HSV1 pneumonia [17]. We compared the results of both studies in an attempt to broaden our knowledge of roentgenographic abnormalities in HSV pneumonia.

Materials and methods

After a search through all the virological data retrieved in our institution between 1992 and the end of 1998 we identified all patients in whom HSV was isolated from material obtained during fiberoptic bronchoscopy (FOB) which also included broncho-alveolar lavage (BAL) and tissue sampling.

Because we were interested mainly in the sole HSVP without cross-infection, we excluded all patients who also had growth of bacteria, other viruses, fungi, and large amounts of yeast. Because of the high predisposition for colonization by *Candida* of critically ill patients, we did not reject patients who only had up to ten colonies per plate besides HSV.

From the virological data 32 patients were found to have a HSV type1 in their lungs detected through FOB. Only 17 patients had a mono-infection with HSV1 (or had also a small amount of yeast as well). From the other 15 patients 7 had cross-infection with bacteria only, 2 with bacteria and yeast, 2 with bacteria and fungus, 1 with fungus only, 1 with yeast only, 1 with Cytomegalic virus (CMV) and yeast and 1 with CMV, bacteria and yeast.

Of the 17 patients with sole HSV 1 pneumonia, ranging in age from 33 to 75 years (mean age 59 years) 12 were men. Underlying causes that may have predisposed these patients to HSVP were present in 16 patients: 4 had non-Hodgkin's lymphoma (all after chemotherapy and 3 had already received bone marrow transplantation), 2 were HIV positive with low CD4 count, 5 had recent major surgery, 3 had leukemia and 2 patients received immunosuppressive medication for kidney transplantation and idiopathic lung fibrosis, respectively. The remaining patient used prednisolone

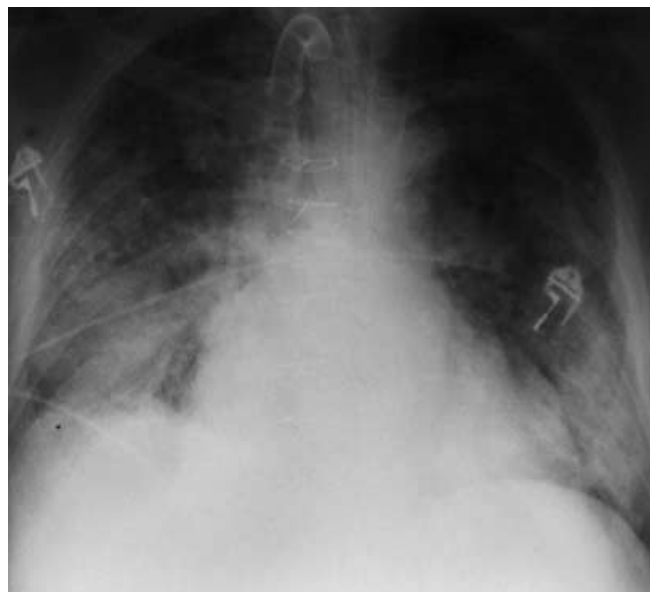


Fig. 1 A 68-year-old male who underwent coronary bypass surgery. Postoperative complications occurred: The patient developed sepsis and later empyema and a lung abscess. Radiograph taken on day of broncho-alveolar lavage (BAL), 40 days after intubation (now tracheal-cannula in situ): bilateral, diffuse alveolar consolidations

for bronchial asthma frequently but was not known to be overtly immunosuppressed. Indications for FOB were fever of unknown origin, unexplained findings on chest radiographs, clinical signs of pneumonia, or respiratory distress of unknown origin.

We studied the conventional chest radiograph made within 24 h of the date of the FOB. Of the 17 patients, 3 were excluded because no chest radiograph was made within 24 h; thus, 14 patients in total were available for study. To determine if there was a relationship with ARDS we used the pathophysiological criteria proposed by The American-European Consensus Conference on ARDS (1994) which states that severe hypoxemia can be defined by an arterial oxygen pressure (PaO_2) divided by the fraction of inspired oxygen (FiO_2). A $\text{PaO}_2:\text{FiO}_2$ ratio of less than 200 indicates ARDS in the absence of left heart failure. The diagnosis of ARDS is strengthened by a pulmonary artery occlusion pressure (PAOP) less than 18 mmHg [21].

The radiographic studies were reviewed independently by two experienced radiologists who arrived at a consensus with the aid of a third radiologist (Figs. 1, 2, 3). Each chest radiograph was evaluated for the following findings: pattern of lung opacities (airspace consolidation, interstitial opacities, or mixed); location (unilateral, bilateral, focal, diffuse) and extent (segmental, lobar, whole lung) of the abnormalities; atelectasis (not-present, lobar, segmental, subsegmental); pleural effusion (not present, moderate, i.e., less than one-third of the hemithorax, large, i.e., more than one-third of the hemithorax). The pattern was described as airspace consolidation in the presence of lobar, segmental, or patchy opacities. Reticular, reticulonodular, and bronchovascular opacities were recorded as interstitial pattern. The use of an endotracheal tube/cannula or Swan-Ganz catheter was also noted.

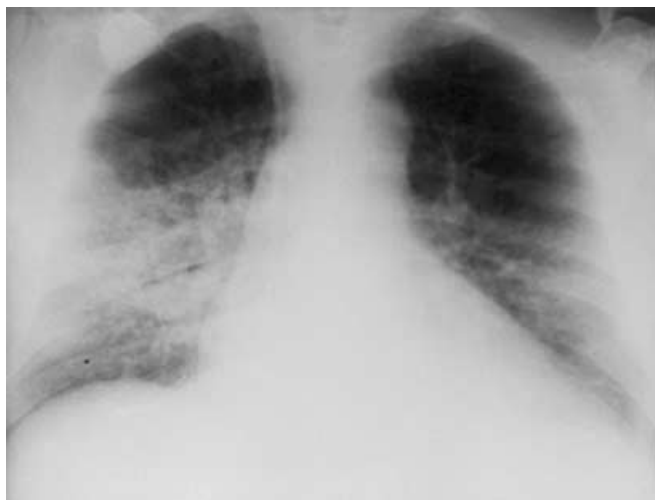


Fig. 2 A 63-year-old male with a history of myelodysplastic syndrome developed acute myeloid leukemia. During treatment with chemotherapy patient became even more immunosuppressed. Broncho-alveolar lavage was performed because of fever and opacities on the chest radiograph. There is a large opacity in the apex of the right lower lobe, but on closer examination bilateral diffuse opacities are seen (e.g., left perihilar region)



Fig. 3 A 75-year-old male operated on for a subarachnoid bleeding. Postoperative cardiac complications occurred with myocardial ischemia leading to forward and backward failure and multi-organ failure. Chest radiograph taken on day of BAL after 20 days of intubation shows a diffuse, bilateral interstitial pattern easily mistaken for pulmonary edema; however, note the small size of the heart and azygos vein

Results

The chest radiographic findings are presented in Table 1. In the majority of patients (12 of 14) lung opacification predominated and was expressed as bilateral, lobar, or diffuse opacities.

Eight of 12 patients showed a pattern that was partly airspace consolidation and partly interstitial opacities (mixed type), three showed only an airspace consolidation, and one an interstitial pattern. The extent of the opacities ranged from at least lobar to almost the entire lung. Diffuse lobar or more extensive opacities were the most commonly recorded abnormalities. We did not notice a predominance for the right or left lung or for a certain lobe. Areas of opacification of more than one lobe were seen in almost half of the patients with an airspace pattern. Lobar atelectasis was present in 3 and (sub)segmental in 2 patients. Pleural effusions were seen in 8 of 14 chest radiographs but only once estimated as a large amount.

Two chest radiographs showed no abnormalities of the lung parenchyma. One of these patients was admitted with progressive respiratory failure and had a history of immunosuppression because of a kidney transplantation, and the other had fever of unknown origin and a history of cardiac arrest and respiratory failure after chemotherapy for acute myeloid leukemia. Twelve patients were intubated and two had in addition a Swan-Ganz catheter. Of 10 intubated patients for whom the $\text{PaO}_2:\text{FiO}_2$ ratio on the same day of the FOB was es-

tablished, 3 had a ratio less than 200. The time from intubation to a positive FOB for HSV1 varied from 1 to 40 days (mean 15 days).

Discussion

Reactivated herpes simplex virus type 1 is often isolated from vesicles of the lip region and oropharynx. Far less commonly HSV1 is found in the lower respiratory tract, although this lower incidence may in part be due to insufficient awareness of HSVP. Prellner et al. showed that HSV1 is a far more common pathogen causing pneumonia than suspected [11].

In the past decade we have encountered herpes simplex virus pneumonia in patients of our hospital, presenting either as a single infection, or in combination with other pathogenic agents. Herpes simplex virus pneumonia was regularly found by BAL, although there were not many occurrences.

Although clinical and pathologic reports of HSVP exist, a search of the international Radiology literature revealed a striking paucity. A description of the radiographic changes in neonatal lung infection caused by HSV type 2 contracted during delivery has been provided by Dominguez et al. [18]. They described a chro-

Table 1 Radiographic features observed in patients with proven mono-infection of herpes simplex virus pneumonia

Radiographic pattern	No. of patients (<i>n</i> = 14)
Pattern of lung opacities	
None/normal X-ray	2
Airspace consolidation	3
Interstitial opacities	1
Mixed	8
Location	
Focal	0
Diffuse	12
Unilateral	0
Bilateral	12
Extent	
Segmental	0
Lobar	6
(Almost) entire lung	6
Atelectasis	
Not present	9
At least Lobar	3
At least segmental	2
Only subsegmental	0
Pleural effusion	
Not present	6
Moderate	7
Large	1

nological development consisting of a normal chest radiograph, interstitial changes, airspace consolidation and, lastly, diffuse consolidation of both lungs; however, extrapolation from type 2 to type 1 HSVP and also from infants to adults is a priori not possible. Nevertheless, radiological similarities can be expected since both viruses produce identical histopathological changes. Other authors have only briefly mention the radiographic findings in studies concerning primarily the pathological and clinical manifestations. Schuller et al. examined 42 patients with HSVP and all chest radiographs were abnormal: 93% showed pulmonary infiltrates, 29% pleural effusion, and 12% atelectasis [19]. Ramsey et al. reported 20 patients with HSVP: 9 had focal abnormalities, 3 multifocal, and 8 diffuse abnormalities [5]. Graham and Snell describe a healthy 20-year-old mother with HSVP and bilateral interstitial infiltrates on chest X-ray [6]. Chabot et al. found 7 patients with HSVP after heart transplantation: 5 of them showed diffuse bilateral changes, either mixed airspace–interstitial or interstitial micronodular [20].

The first major radiological report concerning the conventional chest radiographic patterns of HSVP was written by Aquino et al. [17]. They also describe the abnormalities on CT. The chest radiographs were reviewed within the week prior to the bronchoscopy for each of the 23 patients with HSV1 pneumonia. Twenty-three patients (100%) had patchy segmental or subsegmental airspace opacities, and 11 (48%) had in addition

a lobar distribution of consolidation and ground-glass opacities. Seven patients (30%) had additional reticular opacities. The distribution was diffuse and multifocal in 23 (100%), scattered in 20 (87%), peripheral in 2 (9%), and central in 1 (4%). In 12 patients (52%) pleural effusions were seen. Fifteen patients (63%) were intubated; average duration of intubation prior to FOB was 10.7 days (range 1–18 days).

Fifty percent had a co-existing clinical diagnosis of ARDS. This incidence is much higher than in our group (21%), but Aquino et al. [17] do not appear to have used the strict pathophysiological criteria laid down by the American–European Consensus Conference on ARDS for the diagnosis of this disorder. Since there is overlap in the patient populations susceptible to both ARDS and HSVP, we think that it is important to point out that the bilateral consolidations caused by HSVP can be ascribed to ARDS.

In our study we selected patients only if they had a proven mono-infection with HSV. Our most consistent finding was the presence of bilateral opacities with an airspace or mixed airspace and interstitial pattern. Atelectasis and pleural fluid, although frequently found, were not the dominant radiological features. It should be kept in mind that a large majority of patients in the Intensive Care Department have some amount of pleural fluid and also varying degrees of atelectasis.

Almost all of the radiographic findings in Aquino's [17] study compare very well with our own results with the exception that our series contained two normal chest radiographs. The combination of a normal chest radiograph and a positive BAL may be due to contamination of the BAL sample by the upper airways.

Only 1 patient in our group had a CT scan within a week of the diagnosis so that a comparison of CT scan patterns was not possible.

In summary, diffuse bilateral opacities with predominantly a mixed or an airspace consolidation was the main finding observed in our series of patients with HSV pneumonia. Unilateral consolidation, large atelectasis, and significant amounts of pleural fluid were less frequently observed. Our findings do not support definition of a characteristic pattern for HSV pneumonia on chest radiographs. Awareness of this disease and with the radiographic abnormalities it can cause may nevertheless increase the diagnostic yield in the appropriate setting. This is important because HSV pneumonia benefits from appropriate therapy; however, the definite diagnosis of HSV pneumonia can only be established on the basis of culture of material obtained by broncho-alveolar lavage.

The radiologist may suggest the diagnosis of HSVP particularly when bilateral airspace consolidation or mixed opacities appear in a susceptible group of patients who are not thought to have ARDS or pulmonary edema.

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