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Pneumomediastinum as the Initial Presentation of *Pneumocystis jirovecii* Pneumonia and Influenza A Virus Co-infection in A Newly Diagnosed HIV-infected Patient: A Case Report

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Abstract

Pneumocystis pneumonia (PCP) is the most frequent opportunistic infection in human immunodeficiency virus (HIV)-infected patients. Pneumothorax is the most notorious complication in the disease course of PCP infection, but pneumomediastinum and PCP influenza co-infection in HIV-infected patients has seldom been reported in the literature. The epidemiology, spectrum of clinical presentation, and clinical treatment outcome of co-infection is lacking. Here, we present a patient who had PCP, influenza, and HIV co-infection, with the initial presentation of dyspnea and pneumomediastinum and with a successful treatment outcome. (J Intern Med Taiwan 2021; 32: 142-146)

Key Words: Pneumomediastinum, Human immunodeficiency virus, *Pneumocystis jirovecii* pneumonia, Influenza

Introduction

Pneumothorax is a serious complication of *Pneumocystis* pneumonia (PCP) in human immunodeficiency virus (HIV)-infected patients with an acquired immunodeficiency syndrome (AIDS) status. It may lead to a fatal outcome even when aggressive treatment is administered. However, pneumomediastinum is reported less frequently in HIV-infected patients[1,2]. Meanwhile, co-infection is a constant threat in HIV-infected patients with a low CD4 count. PCP and influenza co-infection is seldom reported in the literature, and the epidemiology and clinical outcome of such patients are lacking. Herein, we present an HIV-infected patient with PCP and influenza A co-infection with pneumomediastinum as the initial presentation, who was treated successfully with an excellent outcome.

Case report

A 22-year-old man who had sex with men came to the Infectious Diseases Outpatient Department (OPD) of our hospital because of intermittent fever for 2 months. At the OPD, oral thrush and ground-

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glass appearance on chest roentgenography were noted. Oral candidiasis, PCP, and HIV infection were suspected. HIV antibody test was performed, and empirical antibiotics were administered. Three days later, he came back to the OPD because of progressive dyspnea. He was admitted to the hospital. Chest roentgenography (Figure 1A) and chest computed tomography revealed pneumomediastinum and subcutaneous emphysema of the neck and chest wall with bilateral ground-glass appearance on the day of admission (day 0) (Figure 2). Under the suspicion of PCP, sputum *Pneumocystis jirovecii* pneumonia (PJP) polymerase chain reaction (PCR) was performed, and sulfamethoxazole/trimethoprim (400/80 mg/vial, 3 vials thrice a day) was administered with hydrocortisone (100 mg/vial, 1 vial thrice a day), but dyspnea persisted. Considering the possibility of co-infection, nasopharyngeal swab for influenza was performed with an influenza rapid test. Pneumonia tests that included pneu-

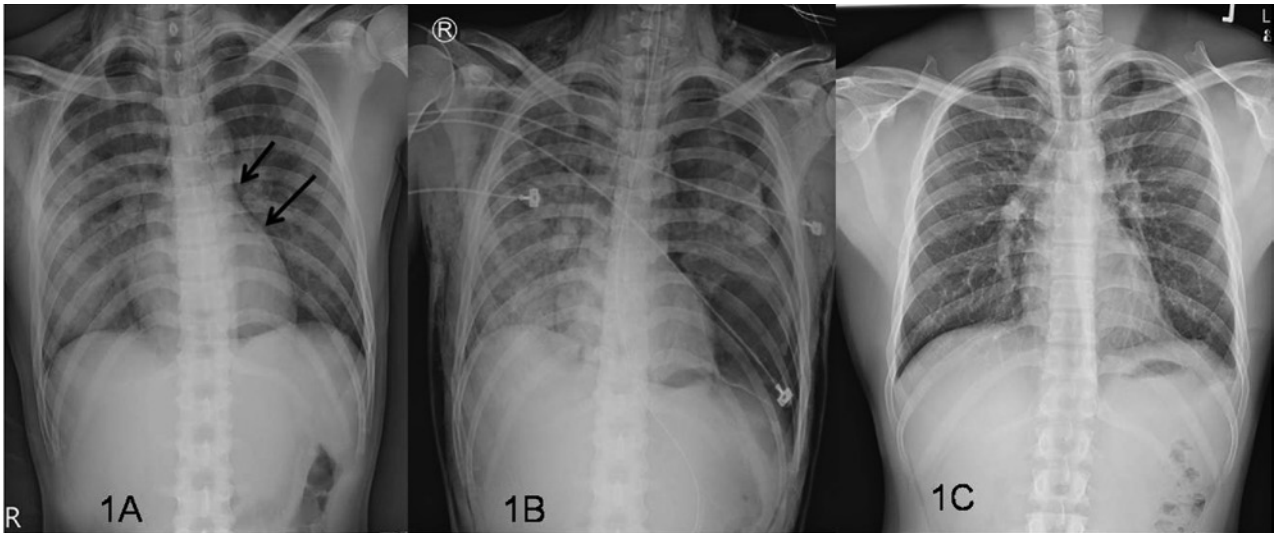

Figure 1. Chest roentgenogram of the patient. Radiolucency line around the heart border is indicated by an arrow on admission day (A). During hospitalization, subsequent pneumothorax occurred in the left lung field (B). Resolution of pneumomediastinum, pneumothorax, and pneumonia after discharge from hospital (C).

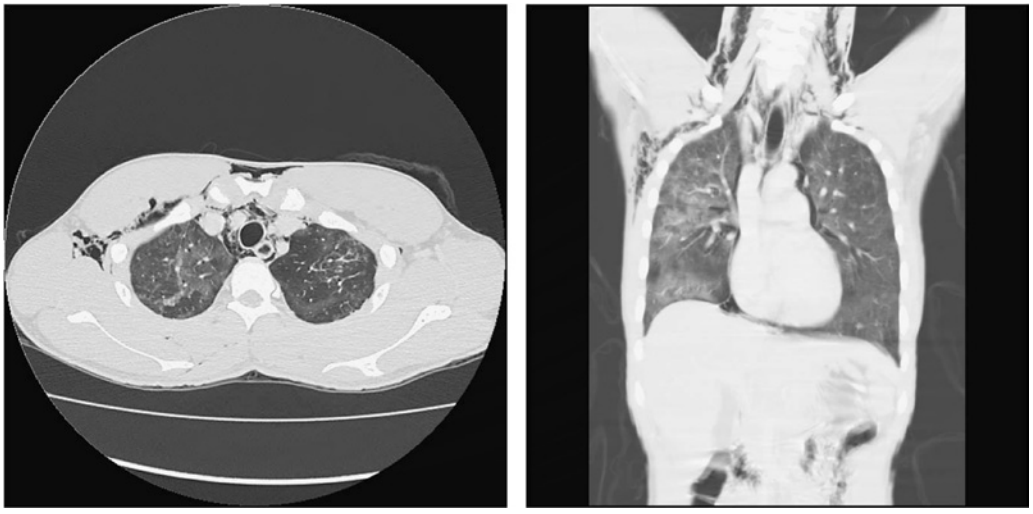

Figure 2. Computed tomography of the patient. Ground-glass appearance of infiltration was noted on bilateral lung fields with prominent free air at the mediastinum and beneath the skin at the neck and thoracic cage area.

mococcus urine antigen, *Legionella* urine antigen, *Mycoplasma* IgM, *Chlamydia* IgM, *Cryptococcus* antigen, *Aspergillus* antigen, and *Cytomegalovirus* (CMV) PCR were performed, and acid-fast staining and sputum culture for *Mycobacterium tuberculosis* were all performed. Soon, PCP was confirmed by sputum PCP PCR and influenza was confirmed by influenza rapid test (QuickVue®, Quidel Corporation, San Diego, CA, USA). Other above-mentioned tests for pneumonia showed negative results. Oseltamivir (75 mg/tablet, 1 tablet twice a day) was administered accordingly. The nasopharyngeal swab sample was sent to Taiwan Centers for Disease Control and Prevention (CDC) for confirmation, and influenza type A was confirmed by PCR testing. The HIV antibody test showed a positive result, and a subsequent HIV western blot test also showed a positive result. The HIV RNA viral load and CD4 count were 80,637 copies/mL and 6 cells/μL, respectively.

Although he underwent aggressive initial surveys and treatments, dyspnea progressed. He was transferred to the intensive care unit, and an endotracheal tube was inserted on day 7. The initial setting of FiO_2 was 80%, and the PaO_2 of arterial blood gas was 191 mmHg. Abacavir/dolutegravir/lamivudine (Triumeq) was administered on day 10. Peramivir (300 mg) infusion (600 mg/day) was administered after 5 days of oseltamivir usage. The FiO_2 was adjusted toward 40% gradually on day 13, but PaO_2 declined to 76 mmHg and reached the level of acute respiratory distress syndrome (ARDS). Although reduced pressure support of mechanical ventilation was provided, pneumothorax occurred on day 19 after admission (Figure 1B). A chest tube was placed for the patient at that point. Because of the worry of delayed healing of the pneumothorax with steroids, hydrocortisone was discontinued. The influenza rapid test of nasopharyngeal samples was performed on days 0, 18, and 23. The test result was positive on day 18 and negative on day 23. During the treatment course, although antiviral and empirical antibiotics for nosocomial bacterial infection were administered, the pneumonia progressed according to chest X-ray findings. Under the suspicion of immune reconstitution inflammatory syndrome (IRIS) and cytokine storm, hydrocortisone 100 mg Q8h IVD was re-added. The condition of the patient improved gradually after steroid use, and the endotracheal tube was extubated after 23 days of intubation. Sulfamethoxazole/trimethoprim was tapered to 2 tablets once daily after the 21-day course of intravenous infusion for secondary prophylaxis. Peramivir was discontinued after 11 days of usage until the influenza rapid test result became negative. Lung air leakage remained after extubation, so a chest tube was placed for a period of time. Urokinase was administered in the pleural space once, and pleurodesis was performed eventually. Before discharge, the pneumomediastinum, subcutaneous emphysema, and pneumothorax totally recovered without any sequelae (Figure 1C). He was discharged after 68 days of admission with an otherwise stable condition. After discharge from the hospital for 9 months, the patient was regularly followed up at the Infectious Diseases OPD for continual antiretroviral therapy, with a CD4 count of 162 cells/μL and viral load of <20 copies/mL.

Discussion

PCP is the most frequent opportunistic infection in AIDS patients. Pneumothorax is a devastating complication of PCP in the advanced disease stage. Pneumomediastinum has seldom been reported as a complication of PCP infection[1]. According to the review by Cheng et al., 11 pneumomediastinum cases in HIV-infected patients were noted until 2012 in the English literature. Of the 11 cases, 9 involved PCP infection only and 2 involved co-infection. Of the 2 cases of co-infection, one involved *Staphylococcus aureus* and the other involved *Nocardia asteroides* complex/*Legionella pneumophila*/*Strep-*

tococcus pneumonia. In these cases, no influenza and PCP co-infection was reported. The overall mortality in this series was 55%[2].

In general, PCP can be treated successfully with sulfamethoxazole/trimethoprim or echinocandins in the post-combined antiretroviral therapy (cART) era[3]. Although PCP can be treated effectively, co-infection is always a clinical concern for treating a patient with an AIDS status. Influenza virus is another important and fatal virus. On influenza virus infection, leukopenia and lower CD4 count below 200 cells/μL may facilitate PCP infection, even in well-controlled HIV-infected patients with a CD4 count >200 cells/μL before influenza infection[4]. Because of limited cases reported in the literature, the impact of influenza superinfection on PCP infection outcome is unknown[5]. Neglect or misdiagnosis of influenza co-infection may increase the possibility of an elevated mortality rate.

Viral shedding of the influenza virus in immunocompetent patients is shorter than immunocompromised patients. According to the study by Memoli et al., the mean shedding is 6.4 days in immunocompetent patients versus 19 days in immunocompromised patients[6]. The study by Vries et al. revealed that 15% of immunocompromised patients with influenza virus infection shed the virus for more than 14 days[7]. The rapid test for influenza virus in the present patient was performed on days 0, 18, and 23, and the result became negative on day 23. In the present case, because of clinical instability and prolonged viral shedding, antiviral therapy with oseltamivir for 5 days and peramivir for 11 days was provided, and it led to resolution of the infection.

On admission, hydrocortisone was administered for PCP with severe hypoxia. Steroids were discontinued once after endotracheal tube intubation and pneumothorax occurrence under consideration of the steroid effect on delaying pneumothorax healing. During the treatment course, although antibiotics and antiviral medications were administered, the pneumonia worsened progressively. Under the suspicion of IRIS, steroids were re-administered, and the pneumonia stabilized and resolved gradually. Although steroid use for influenza pneumonia may be detrimental[8,9], the present patient benefitted from steroid treatment undoubtedly. Thus, in patients with influenza and PCP co-infection, steroid therapy must be used cautiously and must be tailored to individual cases. Although the levels of cytokines, including interleukin-6, were not checked during the treatment course, the resolution of the cytokine storm associated with severe influenza and PCP during the IRIS stage on steroid administration was considered to be the reason for survival of the patient.

In conclusion, pneumomediastinum is an unusual presentation in HIV-infected patients. It may occur in AIDS patients with PCP and influenza co-infection. Timely and adequate treatment with peramivir and steroids for influenza along with medication for PCP co-infection may be crucial for patient survival. Although PCP is the most frequent opportunistic infection in HIV-infected patients, the early detection and timely treatment of co-pathogens, including influenza, may lead to a successful outcome.

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以縱膈腔氣腫為原始表現發生在一個後天免疫缺乏症候群合併肺囊蟲肺炎與A型流感的病人：病例報告

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摘　要

我們在此報告一位以縱膈腔氣腫為原始表現發生在一個後天免疫缺乏症候群合併肺囊蟲肺炎與A型流感的病人，以合併抗生素、延長抗流感病毒藥物及類固醇治療成功的病例報告。