A Rare Case of 4 Ps: Bilateral Pneumothoraces and Pneumomediastinum in Pneumocystis Pneumonia

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ABSTRACT

We report a case of Pneumocystis jirovecii pneumonia (PCP) complicated by bilateral pneumothoraces and pneumomediastinum in a non-human immunodeficiency virus (HIV)- infected patient. This unusual presentation exemplifies the differences in clinical course and presentation in non-HIV versus HIV-infected individuals, and the poor prognosis associated with PCP complicated by pneumothorax or pneumomediastinum. Providers should be aware of the high mortality in patients who develop one, and especially both complications.

KEYWORDS: pneumocystis jirovecii pneumonia, pneumothorax, pneumomediastinum

INTRODUCTION

Pneumocystis jirovecii (carinii) is a yeast-like fungus that classically causes respiratory infections in immunocompromised individuals.[1] The resulting opportunistic infection, Pneumocystis pneumonia (PCP), is associated with significant morbidity and mortality, and is considered one of the AIDS defining illnesses in HIV infections.[2] Spontaneous pneumothorax is uncommon in non-HIV infected individuals with incidence estimated between 0.4–4%, and bilateral pneumothoraces in PCP regardless of HIV status is a rare phenomenon.[3] Pneumomediastinum is another rarely reported complication associated with PCP.[4] Here, we describe a case of PCP in a non-HIV infected individual complicated by bilateral pneumothoraces and pneumomediastinum.

CASE REPORT

A 31-year-old male with a history of Ewing's sarcoma and acute myeloid leukemia in remission, renal cell carcinoma on lenvatinib and everolimus presented with worsening nonproductive cough, dyspnea, and malaise for several days. His cancer course was complicated by optic neuritis from immunotherapy, treated with a several month-long course of prednisone without prophylactic trimethoprim-sulfamethoxazole (TMP/SMX). On admission, the patient was afebrile and tachycardic to the 170's; he was hypoxic on room air, requiring 5 liters/min of oxygen on nasal cannula. Exam revealed bilateral coarse breath sounds and cool extremities. Initial laboratory workup was notable for lactate dehydrogenase of 414 U/L and negative respiratory viral pathogen panel. Chest X-ray (CXR) showed bullous lung disease, ground glass opacities bilaterally, and hypo-density in the superior mediastinum, suggestive of pneumomediastinum. CT angiogram of the chest was negative for pulmonary embolism but confirmed pneumomediastinum. (**Figures 1–3**) He was admitted to the intensive care unit and started on piperacillin-tazobactam, linezolid, azithromycin, TMP/SMX, and methylprednisolone for concern for PCP. At this point, the patient required a high-flow nasal cannula (HFNC) between 20–40 L/min alternating with noninvasive positive pressure ventilation. Bronchoscopy with bronchoalveolar lavage was done and was positive for PCP by direct fluorescent antibody and negative for Legionella, acid-fast bacilli, or malignant cytology. All antibiotics were subsequently stopped except TMP/SMX. Methylprednisolone was switched to prednisone 40 mg daily with a planned taper by 10 mg every five days. On hospital day 7, the patient developed worsening dyspnea. CXR showed new left-sided pneumothorax and small

Figure 1. Chest X-ray HD1 showing bullous lung disease and ground glass opacities in bilateral lung fields

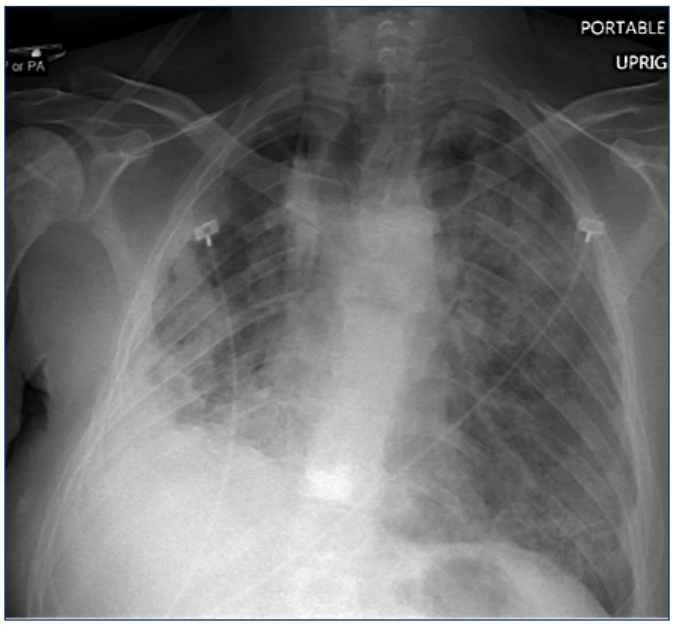


Figure 2. Chest CT on HD 1 showing pneumomediastinum (shown by white arrows)

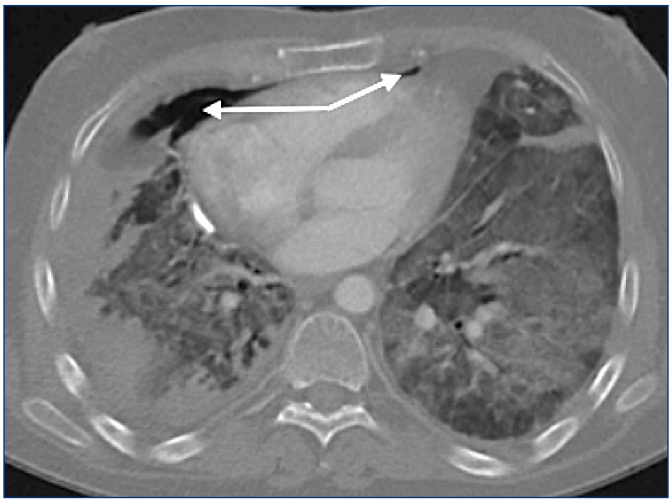
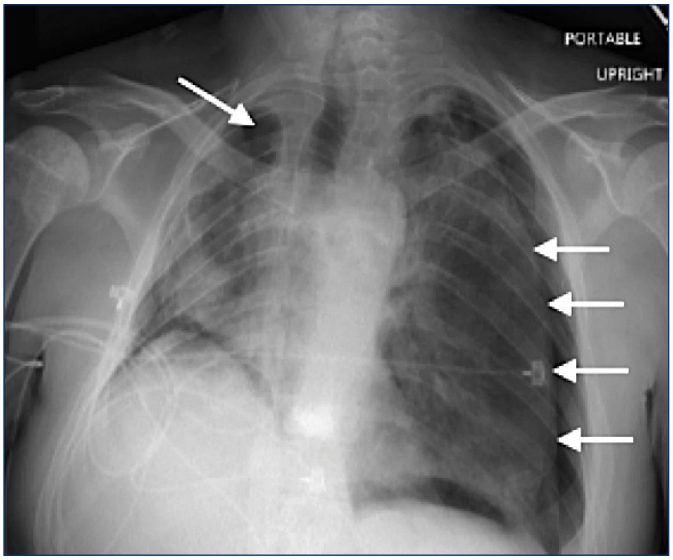


Figure 3. Chest X-ray HD7 showing bilateral pneumothoraces (border of pneumothoraces marked by white arrows)



right-sided pneumothorax. Trimethoprim-sulfamethoxazole and steroid taper were continued. Serial CXRs were done to assess for resolution of pneumothorax.

On day 11, CXR showed worsening left-sided pneumothorax. Chest tubes were placed bilaterally. Despite continuous suction, he failed multiple water seal trials with persistent pneumothoraces on CXR. On day 20, the patient was transferred to another hospital for a second opinion. There he was started on a trial of micafungin for PCP salvage therapy given his overall lack of improvement. He continued to be progressively hypoxemic despite salvage therapy. After discussion with the patient and his family, he was transitioned to comfort measures only. He died on day 4 at the outside hospital.

DISCUSSION

PCP is a potentially devastating illness, especially when complicated by spontaneous pneumothorax or pneumomediastinum. Although classically associated with HIV infections, incidence in non-HIV infected patients has been increasing with increasing prevalence of organ transplantation and widespread use of anti-tumor necrosis factor alpha immunosuppressant medications.[5] The total number of cases of PCP in non-HIV infected patients remains low; however, as PCP prophylaxis appears to be more effective in this population than in HIV cohorts, with an estimated risk reduction of approximately 90%.[6] Chronic steroid use, as in our patient, is an important risk factor, with most studies showing that daily usage of prednisone at 15 mg/day or more for at least one month confers enough risk to warrant PCP prophylaxis.[7] Other risk factors for development of PCP in non-HIV infected individuals include hematologic malignancies, inflammatory disorders, organ transplantations, and solid organ malignancies.[8]

Mortality in non-HIV infected patients with PCP tends to be greater than in the HIV population, with a large meta-analysis reporting a mortality rate of 30.6%.[9] This is also seen in patients admitted to the intensive care unit with one retrospective study reporting mortality rates of 48% versus 17% in non-HIV infected patients and HIV-infected patients, respectively.[10] It has been suggested that mortality tends to be higher in the non-HIV infected population because of ability to mount a greater inflammatory response, including neutrophilic lung inflammation, which may indirectly cause pneumothorax through parenchymal cyst formation.[11] The disease course in HIV patients tends to take a more insidious, subacute clinical course, with symptoms present on average about one month prior to diagnosis.[12] Conversely, the disease course in non-HIV individuals tends to be more rapidly progressive, with symptoms usually present only for days to weeks prior to diagnosis, as demonstrated in our patient.

In addition to inflammation leading to parenchymal pneumatocele formation and rupture, there are a few other theories for spontaneous pneumothorax in PCP. One theory involves subpleural necrosis leading to cavitations, which then form bronchopleural fistulas. Another involves severe inflammation and fibrosis from PCP leading to lung contractures, with slow leakage of air from visceral pleura to the pleural space.[13] Pneumomediastinum in PCP is likely related to cyst rupture, and occurs from free air leak from ruptured alveoli tracking along the pulmonary vessels and the interstitium to the hilum.[14] The incidence of spontaneous pneumothorax and pneumomediastinum is estimated to be between 0.4–4% in non-HIV individuals; co-occurrence is rare in the same individual.[3] Pneumothorax is associated with worse outcomes, with one study citing an increase in mortality up to 50%.[15] We suspect that our patient's ability to mount a greater inflammatory response contributed

to his propensity to develop bullous lung disease, followed by subsequent pneumothorax and pneumomediastinum. Notably, our patient developed both conditions while on chemotherapy with everolimus and levatinib, both medications suppress adaptive immunity, whereas the neutrophilic and macrophage response to pathogens are associated with innate immunity.[16,17]

CONCLUSION

We report an unusual presentation of PCP with bilateral pneumothoraces and pneumomediastinum in a non-HIV infected individual. Both are rare occurrences in non-HIV infected patients, linked to increased mortality compared to HIV positive individuals, likely related to an increased inflammatory response. Clinicians should be aware of the high mortality in patients who have one condition, and especially in patients with both. The importance of prophylaxis with TMP/SMX is crucial for qualified HIV patients as well as non-HIV patients on chronic prednisone greater than 15 mg/day.

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