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CASE REPORT

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A rare case of cytomegalovirus causing respiratory failure and a large pericardial effusion

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ABSTRACT

Cytomegalovirus (CMV) infection is asymptomatic in the majority of immunocompetent patients. However, it can cause severe presentations, particularly in patients who are immunocompromised. We are reporting a rare association between respiratory failure secondary to cavitary pneumonia and a large pericardial effusion due to CMV infection in a patient with human immunodeficiency virus. The patient presented with hypoxic respiratory failure and a large pericardial effusion at risk of tamponade. After extensive investigation, the sole pathogen identified in the patient's bronchoalveolar lavage and pericardial fluid was CMV.

1. Introduction

Cytomegalovirus (CMV) is seroprevalent in a majority of the population around the world but causes symptoms in only a small proportion of infected individuals [1]. Immunocompetent patients are usually asymptomatic, but when symptoms are present, it can resemble a mononucleosis-like infection [2]. Immunocompromised patients can eventually have a severe presentation. The most common presentations of CMV in patients with human immunodeficiency virus (HIV) are retinitis, colitis, and esophagitis. CMV pneumonitis is extremely uncommon [3]. This is a rare case of a severe presentation of CMV in a patient with HIV, in which CMV was responsible for the patient's significant pulmonary and cardiac presentation. The patient presented with hypoxic respiratory failure secondary to cavitary pneumonia and a large pericardial effusion at risk of tamponade. CMV was the only pathogen found in the bronchoalveolar lavage (BAL) and pericardial fluid.

2. Case report

The patient was a 35-year-old African American female with a history of asthma and polysubstance abuse who presented to the emergency department (ED) with severe shortness of breath. She reported that the shortness of breath was progressive over several months and associated with weight loss. She denied a history of HIV infection. The patient's only known home medication was albuterol as needed for asthma. She also reported a history of smoking 10 cigarettes a day and drinking alcohol a couple of times a week.

On physical examination, she was cachectic, ill-appearing and tachypneic with the use of accessory muscles for respiration. Her blood pressure was 88/55 mm Hg, temperature was 37.4°C, pulse rate was 146 beats per minute and regular, oxygen saturation of 70% on room air, and body mass index of 18.9. Lung auscultation revealed bilateral rhonchi. Heart auscultation revealed normal S1 and S2 without significant murmurs or rubs. She was placed on a non-rebreather mask with FiO$_2$ of 100% without improvement of respiratory status and was switched to non-invasive mechanical ventilation. Her status continued to decline, and she underwent endotracheal intubation within an hour of arriving at the ED for hypoxic respiratory failure. SARS-CoV-2 testing done upon arrival in the ED was negative. She tested positive for HIV, and further evaluation revealed an initial viral load of 343,636 copies per milliliter and an absolute CD4 count of 5 cells/μL.

On day 1, a chest radiograph (Figure 1(a)) revealed extensive right lung opacities, most prominent in the right middle lobe. The cardiac silhouette was slightly enlarged. A chest CT scan with intravenous contrast (Figure 2) revealed severe cavitary and partially necrotic opacities in the right upper lobe. There was also a small right pleural effusion and a moderate pericardial effusion. An echocardiogram (Figure 3) revealed a large pericardial effusion, as large as 4.16 cm, with no signs of tamponade.

Initially, she was placed on vancomycin, cefepime, azithromycin, anidulafungin, trimethoprim/sulfamethoxazole (TMP/SXM) and methylprednisolone.
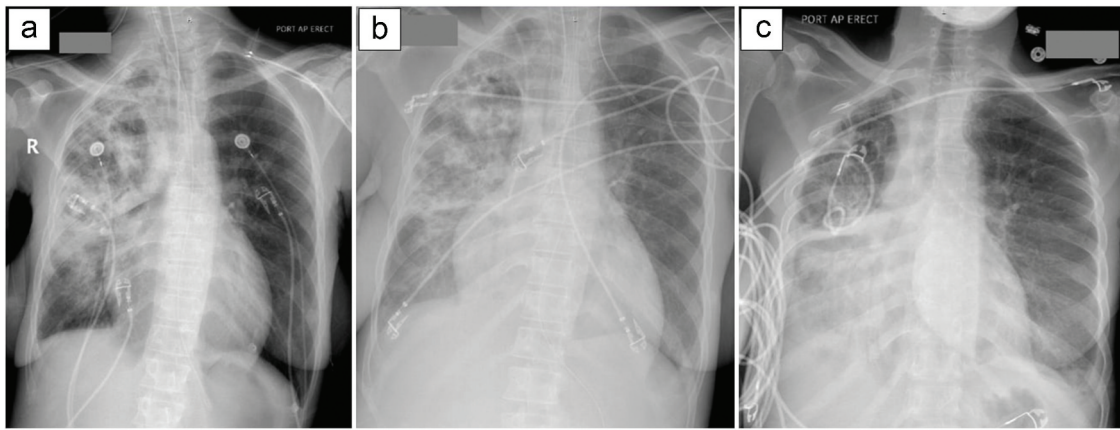
Figure 1. Chest radiographs of CMV pneumonia. (a) Initial chest radiograph with extensive right lung opacities, most prominent in the right middle lobe. (b) Chest radiograph on day 8 with an increase in right-sided infiltrates and new infiltrates at the left lung base. (c) Chest radiograph on day 22 with reduced infiltrates in the right lung field with a moderate overlying pleural effusion.
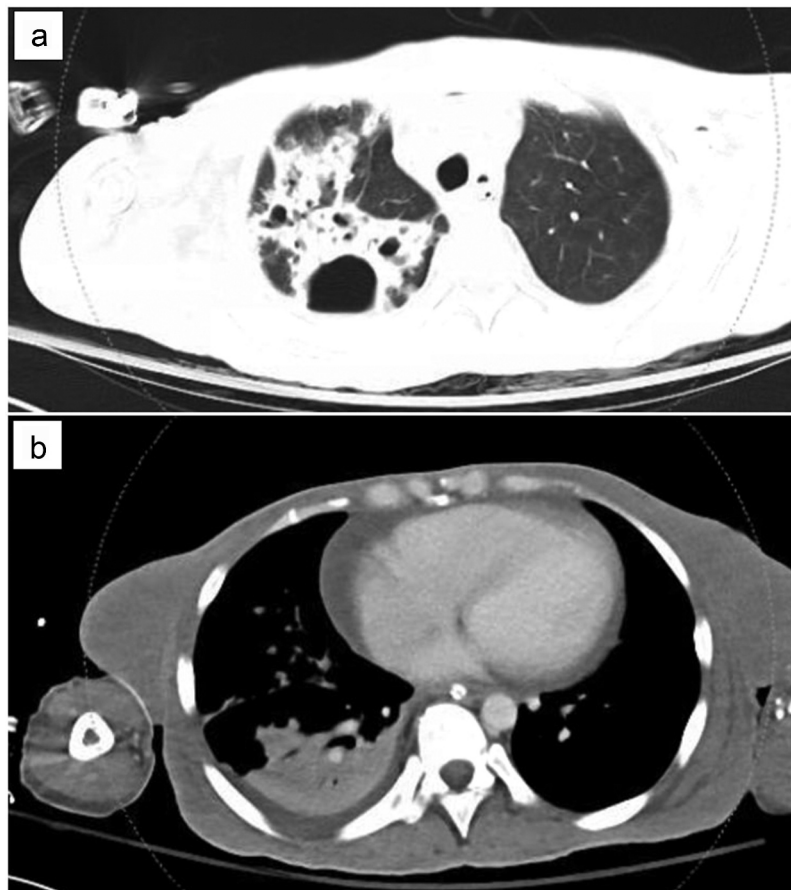

Figure 2. CT scan of chest (axial view). (a) Lung window showing severe cavitary and partially necrotic opacities in the right upper lobe. (b) Soft-tissue window showing small, simple right pleural effusion and a moderate pericardial effusion without evidence of tamponade.

She also required norepinephrine and vasopressin for the first 5 days for hypotension, most likely due to septic shock. On day 5, she underwent bronchoscopy for BAL after tuberculosis was ruled out with three negative sputum acid-fast bacillus smears and a negative polymerase chain reaction (PCR) test. Chest radiography on day 8 (Figure 1(b)) revealed an increase in the right-sided infiltrates and new patchy infiltrates at the left lung base.

On day 13, PCR of the BAL was positive for CMV with CMV DNA of 197,000 IU/mL. Fungal culture of the BAL fluid did grow *Candida albicans*, which was determined to be a colonization. All other tests performed on the BAL (summarized in Table 1) were
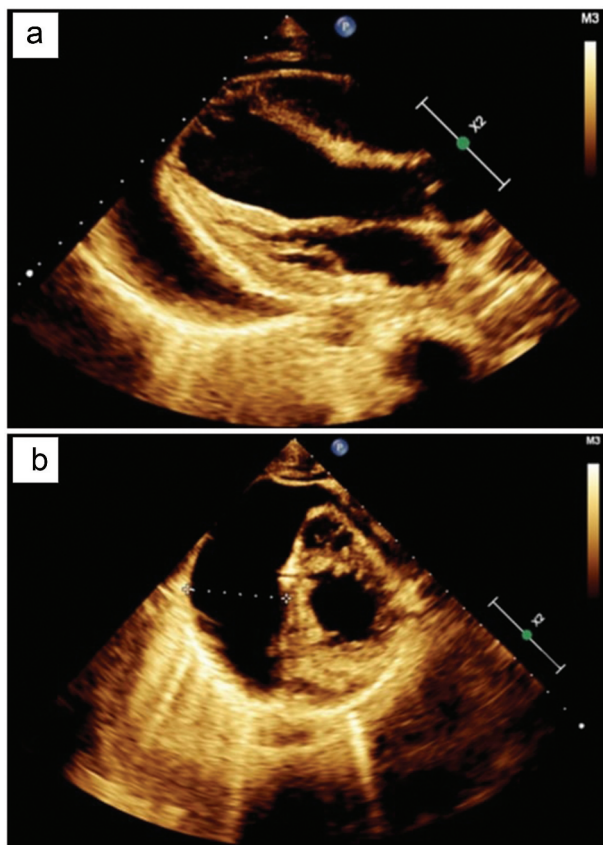
Figure 3. Transthoracic echocardiogram revealing a large pericardial effusion in the left parasternal long-axis (a) and short-axis (b) view.

Table 1. Summary of stain, culture, PCR and cytology results from sputum, BAL fluid and pericardial fluid.

	Sputum	BAL fluid	Pericardial fluid
Gram stain	Mixed respiratory flora	Rare gram-positive cocci in pairs	Negative
Bacterial culture	Normal oral flora	Normal oral flora	Negative
Acid fast stain	Negative	Negative	Negative
Acid fast culture	Negative	Negative	Negative
Fungal culture	Growth of Candida albicans	Growth of Candida albicans	Negative
Cytomegalovirus DNA	N/A	Detected	Detected
Mycobacterium tuberculosis DNA	Not detected	N/A	Not detected
Pneumocystis jiroveci DNA	Not detected	Not detected	N/A
Legionella pneumophila DNA	N/A	Not detected	N/A
Herpes simplex DNA	N/A	Not detected	N/A
Malignant cells identified	N/A	Not identified	Not

BAL: bronchoalveolar lavage; DNA: deoxyribonucleic acid; PCR: polymerase chain reaction; N/A: test was not performed on that sample.

negative. Additionally, tests for Cryptococcus antigen, Histoplasma antigen, Legionella antigen, A. Galactomannan antigen and (1,3)-β-D-glucan were negative. She was started on IV ganciclovir 250 mg twice a day for CMV pneumonia and anti-retroviral therapy for HIV. Anidulafungin, methyl-prednisolone and all other antibiotics were discontinued except for TMP/SXM, which was continued for Pneumocystis jiroveci pneumonia (PJP) prophylaxis. She was extubated on day 13 and switched to high-flow nasal cannula.

On day 17, a follow-up echocardiogram showed that she still had a large circumferential pericardial effusion that had not changed significantly in size since the day of admission. Pericardiocentesis was performed, draining 500 mL of straw-colored fluid. Pericardial fluid analysis was positive for CMV DNA using PCR and negative for adenosine deaminase. All other tests performed on the pericardial fluid (summarized in Table 1) were negative.

A chest radiograph on day 22 (Figure 1(c)) showed reduced infiltrates in the right lung field, with a moderate overlying pleural effusion. Her HIV viral load had decreased to 5,522 RNA copies per milliliter. She was breathing comfortably on room air. She was discharged on oral valganciclovir 900 mg twice a day until her CD4 count improved to over 100 cells/μL,

TMP/SXM for PJP prophylaxis and Biktarvy as antiretroviral therapy.

3. Discussion

The three most common causes of pulmonary infection in patients with HIV are bacterial pneumonia, especially pneumococcal pneumonia, Pneumocystis pneumonia and tuberculosis [4]. Extensive testing was done, and the only pathogen identified in both the BAL fluid and pericardial fluid was CMV. While the fungal culture of the sputum and BAL fluid did grow Candida albicans, it was determined to be colonization rather than infection. First, according to the Infectious Disease Society of America, Candida species are often isolated from the respiratory secretions of mechanically ventilated patients. Furthermore, 'this almost always reflects colonization of the airways and not infection. Candida pneumonia and lung abscess are very uncommon' [5]. Second, the patient tested negative for (1,3)-β-D-glucan by the Fungitell® assay, which has a negative predictive value of 84.8% [6]. Third, the patient improved clinically with treatment for CMV pneumonia alone.

Lung biopsy done to detect CMV cytopathic changes or CMV antigens by immunohistochemistry is the gold standard test to detect CMV pneumonia [7]. This is an invasive procedure that is not routinely done in patients with active infection. Less invasive methods, such as detection of CMV using culture or PCR of BAL fluid, have been investigated to aid in the diagnosis of CMV

pneumonia. Studies have shown that the detection of CMV in BAL fluid can represent asymptomatic viral shedding and not true CMV pneumonia [8,9]. Studies conducted on immunocompromised patients have proposed viral load cut-offs ranging from 500 IU/mL [10] to 500,000 DNA copies/mL [11] to differentiate between asymptomatic viral shedding and CMV pneumonia. Another study failed to find a statistically significant difference in the quantitative DNA in BAL fluid between patients with and without CMV pneumonia [12]. Further investigation is needed to determine if quantitative CMV DNA in BAL fluid can be used to diagnose CMV pneumonia.

Tan et al. [12] proposed a set of criteria for the diagnosis of CMV pneumonitis, which does not require a lung biopsy. The criteria are as follows: a clinical presentation compatible with CMV pneumonitis, the absence of a more likely pathogen for the patient's presentation, and the detection of CMV in the BAL fluid through PCR or culture. Even though the current gold standard to diagnose CMV pneumonia requires a lung biopsy [7], we were confident in our diagnosis of CMV pneumonia based on the patient's presentation and immunocompromised status, the absence of another pathogen that would more likely explain the patient's presentation, and the patient's clinical improvement with ganciclovir therapy. Our clinical reasoning coincided with the criteria that Tan et al. [12] proposed for the diagnosis of CMV pneumonitis.

Pulmonary infections in patients with HIV can present with cavitary lesions in the lungs. In a review of 73 episodes of cavitary lung lesions in patients with HIV, the most common etiologies were fungi, bacteria and mycobacteria [13]. In another report of 25 patients with HIV and cavitary lung lesions, the most common etiologies were bacteria and mycobacteria [14]. While uncommon, CMV was reported to be the cause of cavitary lung lesions in a couple of patients by both Aviram et al. [14] and Lin et al. [13].

According to 'Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV,' CMV pneumonitis is uncommon in patients with HIV [3]. Similarly, in a large study that assessed the prevalence of opportunistic infections and malignancies in 834 individuals with HIV, there were no reports of pulmonary or cardiac manifestations of CMV [15]. The association of CMV causing both pneumonia and pericardial effusion in the same patient is discussed in very few cases [16–19], none of which identified CMV in both the BAL fluid and pericardial fluid. Therefore, pulmonary and cardiac presentations of CMV in patients with HIV are uncommon, even more so when they occur simultaneously.

This case demonstrated the importance of recognizing that CMV can be associated with severe presentations, such as hypoxic respiratory failure, in immunocompromised patients. In our case, bronchoscopy was not performed until day 5 of admission, and CMV was not identified as the most likely pathogen responsible for the patient's presentation until day 13. Empiric therapy with ganciclovir should be considered sooner in immunocompromised patients with respiratory failure where no other pathogen had been identified while awaiting confirmation of diagnosis. The benefits of treatment need to be weighed against the possible adverse effects of ganciclovir. The majority of ganciclovir's adverse effects are hematologic in nature, including thrombocytopenia and leukopenia [2021]. Thrombocytopenia occurs more frequently in patients with cancer chemotherapy or a low creatinine clearance (<20 mL/min). Leukopenia is more common in patients who have a white blood cell count under 6,000 cell/mm^3 [21].

4. Conclusion

CMV is a rare cause of respiratory failure secondary to pneumonia and large pericardial effusion in patients with severe immunosuppression. It can take days to reach a diagnosis of CMV pneumonia because other pathogens need to be ruled out. Empiric therapy with ganciclovir should be considered early in the treatment of critically ill, immunocompromised patients with respiratory failure.

Abbreviations

BAL	bronchoalveolar lavage
CT	computerized tomography
CMV	cytomegalovirus
DNA	deoxyribonucleic acid
ED	emergency department
HIV	Human immunodeficiency virus
PCR	polymerase chain reaction
PJP	*Pneumocystis jiroveci* pneumonia
RNA	ribonucleic acid
TMP/SXM	trimethoprim/sulfamethoxazole

Disclaimer

This paper gives the views of the authors and not necessarily the position of Saint Agnes Hospital or Saba University School of Medicine.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Human ethics

The consent was obtained by all participants in this study.

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