


Dyspnea in an HIV Patient: A Not so Typical Presentation of Lung Adenocarcinoma

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Abstract

Dyspnea in a HIV patient often warrants an extensive workup. The most common etiology of this presentation is likely due to an infectious etiology. However, with the introduction of antiretroviral treatment, non–AIDS-defining illness including malignancies are increasingly being reported. We report the case of a 46-year-old African American female, nonsmoker who presented with dyspnea and found to have pericardial effusion. In patients with HIV presenting with dyspnea, pericardial effusion should be considered among the differential diagnosis, more so in patients in whom infectious etiologies have been ruled out. Further workup, including imaging and biopsy, revealed that our patient had metastatic lung adenocarcinoma. The introduction of antiretroviral treatment has significantly reduced mortality for those with AIDS from AIDS-defining illness and malignancies. However, the incidence of non–AIDS-defining malignancies like lung adenocarcinoma (most common non–AIDS-defining malignancy) is being increasingly reported. Lung adenocarcinoma often presents at a younger age in patients with HIV than the general population. Smoking rates are higher in patients with HIV and may be a contributing factor to the early onset of lung cancer; however, other factors such as long-term medications and immunomodulation in HIV may also play a role. Prognosis is also worse for HIV-positive patients having lung cancer compared with those who are HIV negative, even at a similar stage of cancer.

Keywords

HIV, lung cancer, pericardial effusion, dyspnea in HIV

Introduction

Since the introduction of antiretroviral therapy, the mortality from AIDS has significantly decreased; however, deaths due to other causes (non–AIDS-defining malignancies) continues to be on the rise.¹ In particular, lung cancer is now one of the leading causes of death in HIV.² The risk of developing lung cancer is higher among those with HIV compared with an age-adjusted general population.²

Dyspnea in PLWH (persons living with HIV) has a broad differential diagnosis. Infectious causes include pneumocystis pneumonia, bacterial pneumonias, tuberculosis, *Mycobacterium avium* complex, and viral etiologies like cytomegalovirus pneumonitis. Other causes of dyspnea in PLWH include malignancies like lung cancer and non-Hodgkin's lymphoma (Figure 1).

Case

A 46-year-old African American woman with HIV on ART (antiretroviral therapy) was admitted for progressively

worsening dyspnea. She endorsed orthopnea, ankle swelling, and NYHA (New York Heart Association) class 3 symptoms for 2 weeks prior to admission. On examination, she was tachycardic, normotensive, and hypoxemic with distant heart sounds. She had a palpable left supraclavicular lymph node and multiple axillary lymph nodes. She also had tenderness in her right calf. Her white blood cell count was minimally elevated at 13 500 cells/mm³ with 78% neutrophils. D-Dimer was elevated at 20 µg/mL FEU (fibrinogen equivalent units; normal range: 0.00–0.48 µg/mL FEU). Chest radiograph showed cardiomegaly with no acute infiltrate. Electrocardiogram showed sinus tachycardia. An

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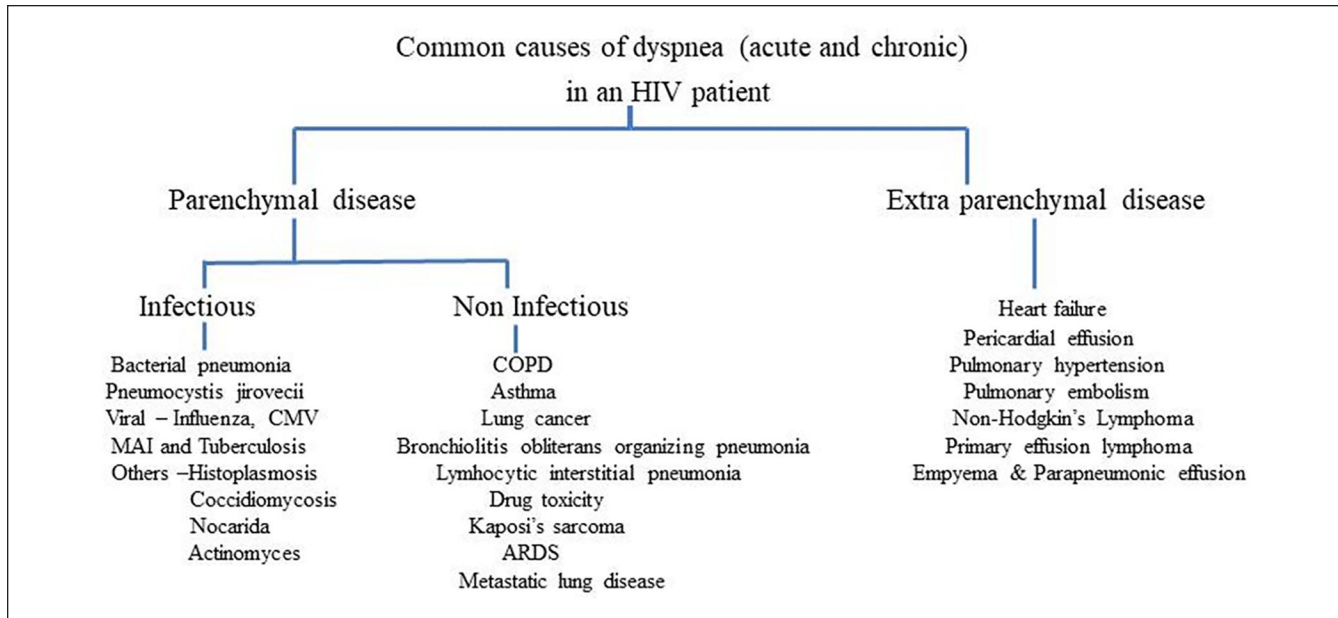


Figure 1. Common causes of dyspnea in PLWH.

echocardiogram revealed moderate pericardial effusion with a normal ejection fraction. A diagnostic and therapeutic pericardiocentesis was performed due to concern for cardiac tamponade as she had an elevated troponin of 0.286 ng/mL (normal range: 0.0-0.034 ng/mL) and distant heart sounds. The pericardiocentesis drained serosanguinous fluid, which showed a normal white blood cells count with negative gram staining, thus ruling out infectious etiology. Venous Doppler of the right lower extremity revealed a deep vein thrombosis and she was started on heparin drip. A chest computed tomography (CT) angiogram showed no pulmonary embolism, but showed right paratracheal adenopathy, right hilar mass, and subcarinal nodes. CT abdomen/pelvis showed bilateral breast masses, bilateral pleural effusions, bilateral adrenal nodules, and vertebral translucency. Her brain magnetic resonance imaging showed 2 lesions, one in the cerebellum and one in the left frontal lobe consistent with metastasis. Her absolute CD4 count was 116 cells/ μ L (normal range: 500-1750 cells/ μ L), CD4 cells percentage was 7% (normal range: 30-61), and T-lymphocyte CD4/CD8 ratio of 0.11 (normal range: 0.86-5.00). She was started on prophylactic antibiotics with trimethoprim-sulfamethoxazole in addition to her antiretroviral treatment. An excision biopsy of the supraclavicular lymph node was consistent with metastatic lung adenocarcinoma with a mucin stain positive, immune staining using TTF-1 (thyroid transcription factor-1) positive and GATA-3 negative (ruling out metastatic breast adenocarcinoma). Pericardial fluid studies showed malignant large epithelioid cells, favoring metastatic adenocarcinoma. Over the course of her hospital stay, the patient continued to have worsening dyspnea, prompting further drainage of her re-accumulating pericardial fluid

with a pericardial window. However, after the procedure was performed, the patient expired as a result of her decompensating status.

Discussion

Dyspnea in an HIV patient has always presented as a paradigm for the clinician. In the absence of any infectious features, other causes including malignancy are to be considered as part of the differential diagnosis. While ART has resulted in reduced mortality for PLWH, this has led to an increase in non-AIDS-defining illness being reported including malignancies and autoimmune disorders.

In PLWH who present with dyspnea, pericardial effusion must be considered as an important differential diagnosis, especially when an infectious workup is negative. Pericardial effusion in an HIV patient warrants further workup for infective etiology and malignancies including lung cancer and lymphoma, often requiring further imaging studies and biopsy.

Our patient who was not a smoker and presented with shortness of breath was diagnosed with metastatic lung cancer at age 46 years, well below the average age of diagnosis of lung cancer (usually age 70 years) in the general population. The mean age at the time of diagnosis for lung cancer in PLWH has been reported to be 45 years.^{1,3} At the time of diagnosis of lung cancer, PLWH are either staged as locally advanced or metastatic (Stages 3 or 4) in 75% to 90% of cases similar to the general population (with no HIV).^{1,3} Non-small cell lung cancer represents around 86% to 94% of the pathology, while small cell lung cancer is reported to be around 5% to 13%.⁴

The pathophysiology and underlying causal mechanism for increased prevalence and earlier onset of lung cancer in HIV is unclear. Prevalence of smoking among those with HIV is higher than the general population,⁵ which could be a contributor. However, the oncogenic role of HIV and the role of chronic immunosuppression warrant more studies. The presence of lung cancer in HIV may be associated with a poor outcome.^{3,6,7} This case allows the clinician to think of noninfectious cause of dyspnea in an HIV patient and to consider non-AIDS-defining malignancies as part of the differential diagnosis.

Treatment

The treatment for lung cancer in PLWH follows the same principle as in patients without HIV. Chemotherapy, radiation, and surgery are the options depending on the staging at diagnosis. The prognosis for lung cancer is worse in patients who are HIV positive than the general population.^{6,7} Irrespective of the staging at time of diagnosis, median survival for those with HIV diagnosed with lung cancer is 4.5 months (range: 3-9) as opposed to 10 months (range: 4-12.5) in age-matched HIV-negative controls.³ CD4 counts and AIDS diagnosis in PLWH did not influence prognosis of lung cancer.^{8,9} With regard to immune check point inhibitors and their use in HIV, a systematic review looking at the safety and efficacy of immune check point inhibitors with HIV infection and advanced stage cancer were associated with no new safety signals.¹⁰ Immune check point inhibitors are considered safe and efficacious for PLWH with cancer as the general population.¹⁰ The 2018 National Cancer Comprehensive Network (NCCN) guidelines for non-small cell lung cancer in PLWH recommends making decisions for treatment based on the performance status of the patient, taking into account poor performance status could be secondary to HIV not being treated and ART may improve poor performance status.¹¹ Furthermore, smoking cessation should be offered to PLWH and lung cancer.

HIV Treatment and Monitoring During Cancer Therapy

As per 2018, NCCN guidelines for cancer in PLWH, ART should be initiated and maintained (ideally by an HIV specialist in collaboration with the oncology team).¹¹ If the patient is already on ART, current recommendations are to continue ART usage.¹¹ For patients who have not yet started ART, recommendations are to initiate ART at least 7 days before the start of cancer treatment or long enough so that after cancer therapy has been started, one is able to distinguish between adverse effects of chemotherapy and ART.¹¹

HIV viral load and CD4⁺ T-cell monitoring should be performed as per the normal schedule for PLWH.¹² More frequent HIV viral load testing such as once a month for the first 3 months, followed by testing every 3 months may be

considered if systemic cancer therapy is needed (especially those known to cause lymphocytopenia).¹³ If cancer therapy causes lymphocytopenia, HIV viral load monitoring is considered a better indicator of HIV than CD4⁺ T-cell count.¹¹

Screening

Lung cancer screening is based on current recommendations from the National Lung Screening Trial (NLST), which demonstrated that annual low-dose CT can lead to a 20% reduction in lung cancer mortality through early detection and treatment.¹⁴ It was based on the results of NLST, that the Centers for Medicare and Medicaid services initiated coverage for lung cancer screening in those who met criteria (age 55-75 years, 30-pack years of smoking, current smoker, or quit within the past 15 years). The United States Preventive Service Task Force also recommended annual lung cancer screening for those who met criteria based on the NLST. However, PLWH were not included in the NLST and were not part of the guideline recommendations.

There is limited clinical trial data evaluating lung cancer screening in HIV-infected smokers.¹⁵ In a population study that looked at benefits and harms of lung cancer screening in PLWH, Kong et al found that PLWH who were smokers with CD4⁺ count of at least 500 cells/ μ L who undergo lung cancer screening would have similar mortality benefit as the general population (who met criteria per NLST).¹⁵ The study is limited as mentioned by the authors of the study itself, by the need for 100% screening adherence rate.¹⁵ The national adherence rate for low-dose CT is still in early stages and unknown, and thus, the adherence rate in the real-world setting is limited.¹⁵ The 2018 NCCN guidelines for lung cancer in PLWH recommends screening for lung cancer to be performed in PLWH based on the same criteria used in the general population.¹¹ However, for PLWH who are nonsmokers as in our patient, there is no conclusive data on screening for lung cancer prompting the need for further trials in PLWH.

Authors' Note

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Informed consent for patient information to be published in this article was not obtained because the patient passed away.

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