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Newly Diagnosed AIDS with Multiple Opportunistic Infections Despite a Recent Negative Rapid HIV Test

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Newly Diagnosed AIDS with Multiple Opportunistic Infections Despite a Recent Negative Rapid HIV Test

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Background

Human Immunodeficiency Virus (HIV) is a fairly prevalent disease in the United States, with an estimated 1 million persons infected with HIV-1.[1] Despite a decrease in Acquired Immunodeficiency Syndrome (AIDS), the prevalence of HIV is increasing, which has led to recent changes in HIV testing guidelines.[2] Newly diagnosed patients should ideally be linked to care and receive intervention and antiretroviral therapy (ART) allowing them to maintain a near normal life expectancy.

Case Presentation

The patient is a 23-year-old African American male with no significant past medical history. He presented to the emergency department (ED) with fevers, weakness, worsening right-sided chest pain, and shortness of breath associated with a productive cough. When he presented with similar symptoms two weeks ago, he was treated for pneumonia with azithromycin. Symptoms initially improved but then worsened five days prior to returning to the ED. He had odynophagia for the last three weeks causing him to avoid solid foods. Additionally, he reported loss of vision in his right eye for two months which started as blurriness but progressed to only appreciating light versus dark. Left eye vision was intact.

He took no chronic medications and denied drug allergies. Surgical and family history was non-contributory. He rarely drank alcohol and denied tobacco or drug use. He is homosexual and became sexually active at the age of fourteen with inconsistent condom use. He reported a negative rapid HIV test at a local clinic one month ago and his last sexual contact was three months prior to presentation.

Investigations

On physical exam, the patient's vitals were temperature of 97.6°F, heart rate 101 bpm, blood pressure 133/76 mmHg, respiratory rate 18 bpm, pulse oximetry 98% on room air. Head and neck exam revealed oral thrush and a nonreactive right pupil. Confrontation of visual fields revealed lack of vision in all four quadrants of the right eye. Eyes were anicteric and without conjunctival injection. Cardiovascular exam revealed mild tachycardia but was otherwise normal. Lungs were clear to auscultation. Abdomen exam was unremarkable. He had no lymphadenopathy and the rest of his physical exam was normal.

Lab work was significant for a hemoglobin of 11.6 g/dL, mean corpuscular volume of 78 fL, RDW 15.5%, and lactate dehydrogenase of 581 IU/L. Comprehensive metabolic panel was within normal limits. Chest X-ray revealed patchy bilateral perihilar interstitial infiltrates, more progressed compared to two weeks prior. A rapid HIV test in the ED was positive. CT of the chest showed bilateral patchy, confluent areas of ground glass opacity with perihilar predominance involving all lobes relatively sparing the bases.

Differential Diagnoses

Given his newly diagnosed HIV infection, differential diagnosis included community acquired pneumonia (CAP), Pneumocystis jirovecii pneumonia (PCP), opportunistic viral pneumonia, fungal pneumonia, Mycobacterium infection. His odynophagia was thought to be secondary to esophagitis, likely from Candida albicans, Cytomegalovirus (CMV), or Herpes Simplex Virus (HSV). Possible causes of vision loss included CMV retinitis, toxoplasma retinochoroiditis, and Varicella Zoster Virus Retinitis.

Treatment

Infectious Disease (ID) was consulted, and he was started on empiric moxifloxacin to cover for CAP, including atypical pathogens. He was also started on IV pentamidine for possible PCP. Pentamidine was used secondary to a hospital shortage of IV trimethoprim-sulfamethoxazole (TMP-SMX). Additionally, he was received IV ganciclovir to empirically treat CMV retinitis and possible CMV or HSV esophagitis. He was started on fluconazole to treat thrush and possible candida esophagitis.

His rapid HIV antigen/antibody combination test was positive and confirmed by Western Blot. His CD4 count was 41 cells/mcL, establishing a diagnosis of AIDS. The genotype revealed wild type HIV-1 with a viral load of 3.68 million copies/mL.

Upon admission, Ophthalmology performed a dilated eye exam, which revealed total retinal necrosis of the right eye. There was necrosis and fibrosis of the macula, peripheral retinal necrosis, as well as "frosted branch" retinitis and hemorrhage with "brush fire" appearance. These exam findings combined with a CD4 count less than 50 cells/mcL were consistent with CMV retinitis, and visual prognosis was poor given diffuse necrosis that progressed for two months. Exam of the left eye revealed mild cotton wool spots which could represent either early CMV retinitis versus HIV retinopathy. For induction treatment, he was continued on IV ganciclovir (eventually changed to oral valganciclovir).

His respiratory symptoms slowly began to improve with antibiotics. Bronchoscopy revealed minimal non-purulent secretions. Cultures from bronchoalveolar lavage (BAL) were negative for acid fast bacilli, respiratory viruses (including

influenza A, B), and bacteria. Fungal culture showed light growth of Candida albicans, and cytology with silver stain was positive for PCP. Treatment was narrowed to IV pentamidine until he was able to tolerate oral treatment doses of TMP-SMX.

He was maintained on fluconazole for thrush. For his esophagitis, endoscopy was deferred as he was already on fluconazole for Candida infection as well as IV ganciclovir for treatment CMV retinitis, which would also treat concomitant CMV or HSV esophagitis.

Outcome And Follow-Up

His symptoms began to improve significantly. After his esophagitis resolved, he was transitioned to oral medications to complete treatment of his multiple opportunistic infections. He was discharged from the hospital to finish treatment at home and follow up with his ID physician later that week to initiate ART.

Discussion

This case illustrates that despite improved testing techniques, it is still possible for patients to present with new diagnoses of HIV in late stages. Moreover, false negative screening tests are still possible, and patients can present with new HIV/AIDS via multiple simultaneous opportunistic infections. Additionally, it reinforces treatment of various opportunistic infections.

This patient presented with a CD4 count of 41 cells/mcL but had a negative HIV test one month prior. This represents either seronegative chronic HIV infection or chronic infection with a false negative enzyme immunoassay (EIA) and failure to detect the antibody. Alternatively, it may be an atypical instance of acute infection prior to seroconversion with the CD4 count falling dramatically low before recovering to the typical 600-700 cells/mcL.[3] The latter scenario of an acute infection would place the primary HIV infection at roughly 6 weeks prior to admission, which is less likely since visual symptoms began at least 8 weeks prior to admission.[3,4] A final possibility is fulminant HIV. Given his long standing risk factors and several months of visual symptoms (which occur at advanced immunosuppression), he likely had chronic HIV that was not detected.

The CDC recommends use of rapid HIV tests so more patients obtain their results.[4] Many outpatient facilities use the third generation EIA, capable of detecting HIV antibodies as early as three weeks after infection.[5,6] All commercially used tests have excellent sensitivities (>99%) for detection of HIV antibodies, and many can detect them even before the traditional Western blot confirmation test can, yielding pseudo-false positive results that require repeat testing.[5] Although these screening tests have excellent performance, their sensitivities are not 100%. There are several reported incidences of false negative EIA tests secondary to immune dysfunction and impaired humoral response, delay to seroconversion following initiation of ART, as well as fulminant HIV infection.[7-11]

This case demonstrates the need for better access to care and earlier intervention. Unfortunately, this young man's retinal necrosis was so advanced that he will likely never recover vision in his right eye. Had his HIV been diagnosed earlier, his multiple infections and vision loss may have been prevented. Due to an increasing prevalence of HIV, the 2006 revised CDC guidelines for HIV testing recommend screening for patients in all settings in an opt-out fashion, at least annual testing for those at higher risk, and screening to become overall more routine and not require separate consent.[4] A new US Preventative Services Task Force (USPSTF) draft recommends screening all adults age 15 to 65, with more frequent testing in high risk individuals.[12]

PCP usually occurs in HIV patients with CD4 counts less than 200 cells/mcL. Patients typically develop fever, progressive dyspnea, nonproductive cough, chest discomfort, and uncommonly blebs, cysts, and pneumothorax. Severe cases are characterized by hypoxemia. Imaging usually demonstrates diffuse, bilateral, interstitial infiltrates. Diagnosis requires induced sputum or BAL histopathologic confirmation. Treatment of choice is TMP-SMX orally or parenterally in severe cases and when patients cannot tolerate oral medications. In cases of drug intolerance, IV pentamidine is the preferred treatment. Patients with moderate-severe disease, PaO2 less than 70 mmHg or A-a gradient > 35 mmHg should receive corticosteroids. Treatment should last 21 days, then TMP-SMX should be decreased to prophylactic dosing. Additionally, ART should be initiated within two weeks if not already started.[13]

CMV disease is usually in patients with HIV and CD4 counts less than 50 cells/mcL. CMV retinitis is a necrotizing retinitis that often begins unilaterally, but without treatment, viremic dissemination causes bilateral retinitis. Symptoms include scotoma, floaters, and visual field defects. Visual acuity decreases with central retinal lesions. Diagnosis is made by an ophthalmologist during a dilated eye exam with recognition of characteristic fluffy yellow-white retinal lesions and possible intra-retinal hemorrhage. Treatment for mild disease is typically oral valganciclovir. Moderate-severe disease is treated with intraocular implant of ganciclovir plus oral valganciclovir or iv ganciclovir alone. Induction phase is 14-21 days followed by maintenance with lower dose valganciclovir and regular ophthalmologic exams to detect relapse or immune recovery uveitis. Maintenance can be discontinued after six months of sustained quiescent retinitis and CD4 counts over 100 cells/mcL.[13]

Esophagitis is characterized by odynophagia and retrosternal pain. In HIV patients, it is reasonable to empirically treat for candida, especially with the presence of oral thrush, and perform endoscopy if symptoms do not improve after 3-5 days. Treatment of choice for candida esophagitis is systemic treatment for 14-21 days with fluconazole. CMV esophagitis is diagnosed by endoscopy and biopsy and is treated with IV ganciclovir or oral valganciclovir if tolerated for 21 days or until symptoms resolve. HSV esophagitis is treated with IV acyclovir (orally if tolerated) for 14-21 days.[13]

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Key Points

In accordance with revised guidelines, HIV testing should be routine, particularly in patients who are high risk. Clinical judgment should increase index of suspicion for further HIV testing such as nucleic acid amplification, as there are rare cases of seronegative AIDS as wells as false negatives despite excellent sensitivities.

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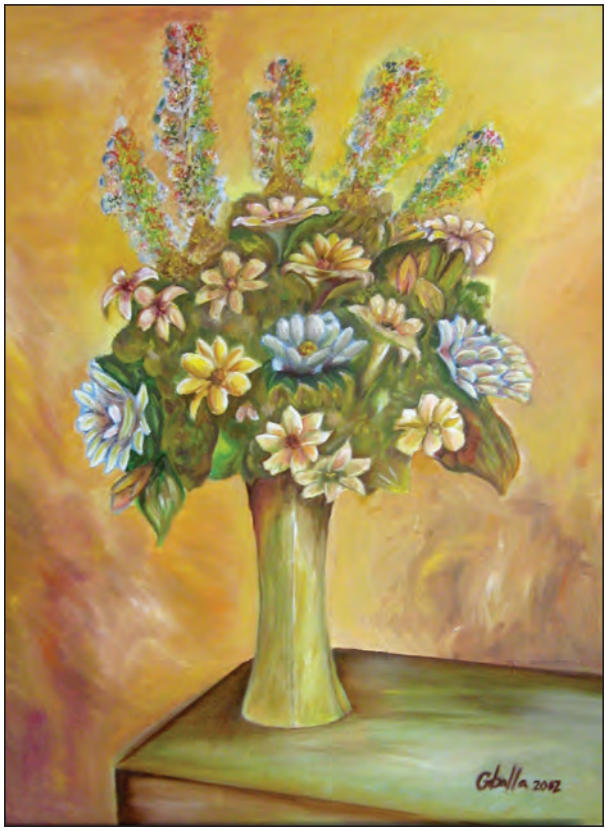
"Flower Vase"
painting by Mahmoud Gaballa



"Pretty in Pink"
photograph by Rina R. Shah