



A CASE OF HIV AIDS - EXISTENCE OF FOUR SYMBIOTIC OPPORTUNISTIC CO INFECTIONS

Internal Medicine

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ABSTRACT

HIV/AIDS is a global health issue with a significant impact on morbidity and mortality worldwide. Opportunistic infections are a major cause of morbidity and mortality in HIV/AIDS patients particularly those not who are not receiving antiretroviral therapy (ART). The presence of multiple opportunistic infections in an individual is not uncommon, and these infections may often have a symbiotic relationship, where the presence of one infection can lead to the development of another, leading to a more severe disease course. We present a case of a 31-year-old female, recently diagnosed with HIV/AIDS not on ART who's diagnosis was complicated by the existence of multiple opportunistic infections including pulmonary tuberculosis, pneumocystis pneumonia, herpes genitalis and vulvovaginal candidiasis. This case report highlights the importance of early diagnosis and prompt management of these infections in HIV/AIDS patients to improve their overall outcomes. A multidisciplinary approach is necessary to manage patients with multiple opportunistic co infections, which requires close collaboration between different medical specialties. This case report also emphasises the need for a high index of suspicion for opportunistic infections in patients with HIV/AIDS, especially in resource limited settings, where the burden of opportunistic infections is high.

KEYWORDS

HIV, AIDS, opportunistic infections

INTRODUCTION

Opportunistic infections are a group of infections that tend to afflict individuals with a weakened immune system, such as those with HIV/AIDS. These infections are caused by microorganisms that are typically benign in individuals with a robust immune system but can cause severe disease in immunocompromised individuals. (1,2) The CD4 count, a key marker of immune function in people with HIV/AIDS, plays a crucial role in the development of OIs. As the HIV virus targets and destroys CD4 cells, the CD4 count decreases, increasing the individual's susceptibility to OIs (3)(4). The risk of developing OIs in individuals with HIV/AIDS is directly related to their CD4 count. Those with a CD4 count below 200 cells/mm³ are at high risk of developing OIs, whereas those with a count above 500 cells/mm³ have a low risk (1)(3)(4). Pneumocystis jirovecii pneumonia, tuberculosis, candidiasis, cryptococcal meningitis, and toxoplasmosis are some of the most common OIs observed in people with HIV/AIDS. These infections can be life-threatening if not promptly diagnosed and treated (1)(2)(5). There is a limited amount of literature specifically addressing the combination of these opportunistic infections in a patient of HIV/AIDS and their management. Antiretroviral therapy (ART) is the primary treatment for HIV/AIDS and can enhance immune function and lower the risk of OIs. Additionally, prophylactic treatment can be administered to individuals with a low CD4 count to prevent the development of certain OIs (1)(3)(4).

CASE PRESENTATION

A 31-year-old female, who worked as a farm labourer, presented to our hospital with a 5-month history of intermittent undocumented low-grade fever, associated with evening rise of temperature, and easy fatigability. In the initial few months, she used to have fever every 3-4 days which then became daily in the last 1 month. She also complained of gradually progressive shortness of breath for 4 months initially on exertion, which worsened over the last 1 month to breathlessness on walking less than 100m associated with dry cough for the last 10 days. Further history revealed dysuria, difficulty in sexual intercourse with painful lesions in the genital area, and whitish discharge per vagina associated with itching for 2 months.

On examination, she had a low-grade fever, tachypnea, and decreased air entry bilaterally on lung auscultation with oxygen saturation of 94% on room air. Furthermore, multiple painful ulcers with erythematous bases were present over her genital area, the largest measuring 3*3cm with whitish curdy non-foul-smelling discharge covering the labia minora.

During her hospitalization, she had worsening dyspnea with new-onset oxygen requirement.

INVESTIGATIONS

On routine investigations, she was diagnosed with HIV 1 infection with a CD4 count of 139. Baseline investigations revealed anemia with raised counts. peripheral smear revealed normocytic normochromic anemia. Workups for tropical fever infections such as Dengue, Malaria, Scrub typhus, Leptospira, and Typhoid were negative. Arterial blood gas analysis showed normal anion gap metabolic acidosis with lactic acidosis and type 1 respiratory failure. Ultrasonography of the abdomen showed hepatosplenomegaly. Chest X-ray showed bilateral diffuse miliary mottling with bilateral pleural effusion and bronchoalveolar lavage GeneXpert confirmed pulmonary tuberculosis. On the seventh day of admission, she had worsening tachypnea with new onset oxygen requirement. Lab investigations showed an elevated LDH, and arterial blood gas analysis revealed severe hypoxemia with (A-a) gradient of 42. High resolution computed tomography of thorax (HRCT) demonstrated diffuse bilateral ground glass opacities.

INVESTIGATIONS	Normal range and units	Day 1 of admission	Day 3	Day 8	Day 12	Day 15
Hemoglobin	13-17 g/dl	5.8	7.2	7.3	8.5	7.9
Total leucocyte count	4-11 x 10 ³ /uL	10.23	6.45	5.28	4.75	2.16
Neutrophil	40-70%	84	91	83	81	83.8
Lymphocyte	20-40%	10	6.7	10	14.7	12.5
Monocyte	2-8%	3.7	1.2	2.5	3.4	3.2
Eosinophil	1-6%	0.6	0		0.2	0
Basophil	<2%	0.1	0.2		0.2	0
Platelet	150-400x10 ³ /uL	225x10 ³ /uL	243x10 ³ /uL	309x10 ³ /uL	303x10 ³ /uL	266x10 ³ /uL
Total bilirubin	0.3-1.2 mg/dl	1.78			1.45	1.37
Serum glutamic oxaloacetic transaminase (SGOT)	0-50 U/L	58			78	176
Serum glutamate pyruvate transaminase (SGPT)	0-50 U/L	64			81	116

Alkaline phosphatase (ALP)	30-120 U/L	1819			2140	1837
Gamma-glutamyl transferase (GGT)	0-55 U/L	653			1140	985
Urea	17-43 mg/dl	32			21	
Creatinine	0.72- 1.18 mg/dl	0.43			0.44	

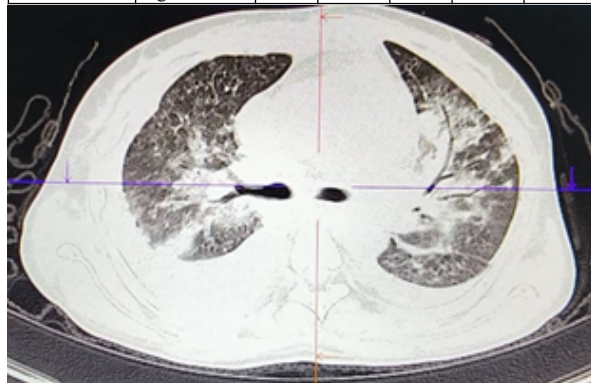


IMAGE 1: Bilateral lung areas of consolidation and air bronchograms, along with interspersed areas of ground glass opacities.

Radiological Investigations:

Contrast enhanced computed tomography (CECT) thorax and abdomen

- Features of ARDS in background of active infective changes in bilateral lungs.
- Bilateral pleural effusion, pericardial effusion.
- Hepatosplenomegaly with granulomas in spleen with multiple enlarged mesenteric, retroperitoneal lymph nodes - likely disseminated TB.
- Cervical lymphadenitis.

Magnetic resonance cholangiopancreatography (MRCP): normal study

Microbiological investigations:

Urine culture: Escherichia coli sensitive to (amikacin, nitrofurantoin, ampicillin salbactam)

Blood culture: Sterile

Sputum culture: normal respiratory flora

Stool culture: no growth of parasitic organism

Treponema pallidum: negative

Flocculation test: non-reactive

BAL GeneXpert: MTB detected; rifampicin resistance not detected

BAL culture: no growth

Pleural fluid culture: sterile

Pleural fluid GeneXpert: negative

TREATMENT AND FOLLOW UP:

The diagnosis of HIV with pulmonary tuberculosis, Pneumocystis carinii pneumonia, herpes genitalis and vulvovaginal candidiasis was made. Due to risk of IRIS, ART was delayed and she was started on standard anti-tubercular therapy. In view of PCP pneumonia, she was started on a combination of trimethoprim-sulfamethoxazole and steroids and showed a significant improvement in her symptoms and oxygenation within 48 hours. She was treated with fluconazole and acyclovir for her herpes genitalis and vulvovaginal candidiasis. The lesions resolved within a week. She developed a cholestatic pattern of liver injury, hence modified ATT (streptomycin, levofloxacin and ethambutol) was initiated.

Her clinical condition improved during the course of hospital stay, and she was discharged after 3 weeks of hospitalization. During her first follow up visit after 1 week, she was started on anti retroviral therapy. During her subsequent follow-up visits, she showed significant improvement in her clinical status.

DISCUSSION

HIV is a major public health problem worldwide, with Sub Saharan Africa bearing the highest burden of the disease. The presence of HIV predisposes individuals at an increased risk of developing wide range of opportunistic infections, which are often severe and potentially fatal, particularly in patients with advanced HIV disease who are not receiving anti retro viral therapy. A systemic review and meta-analysis of 126 studies and 491,608 HIV infected persons published from January 1990 to 21 November 2013 to estimate the incidence of key OIs in HIV infected individuals in low and middle income countries including Sub Saharan Africa, Asia and Latin America and to evaluate the magnitude of effect of ART on the incidence of these OIs during and after first year of treatment, found that the most common OIs in ART-naïve participants were oral candidiasis (19.1%), unspecified TB (10.0%), herpes zoster (9.4%), PTB 9.0), and bacterial pneumonia (6.1%). There was a major reduction in risk for most OIs with ART use with the greatest effect seen in the first year of treatment. (6)

Opportunistic infections are a significant cause of morbidity and mortality in HIV patients and their occurrence is usually linked to the degree of immunosuppression as measured by the CD4 count. (7) The presence of these infections in a single patient can pose a significant challenge to the healthcare provider, as each infection requires specific management strategies. The presented case highlights the existence of multiple symbiotic opportunistic co infections in a newly diagnosed HIV/AIDS patient all of which were diagnosed during the hospital stay. The delay in seeking medical attention may have contributed to the development of multiple opportunistic infections and severity of the patient's condition.

TB is the leading cause of death among people living with HIV (PLHIV) worldwide and it is estimated that one third of people living with HIV are coinfecting with TB. Among individuals with TB infection, the risk of developing active TB is much higher among those who also have HIV, and this risk increases as immune deficiency worsens. (8) The interaction between HIV and TB is complex, and coinfecting individuals often present with atypical clinical features, such as extrapulmonary TB, disseminated TB, or TB with a negative sputum smear (9). The management of HIV/TB coinfection is challenging, and treatment requires careful consideration of drug-drug interactions and potential side effects. In cases of severe immunosuppression, such as the one described in this case report, the initiation of ART should be delayed until the patient's TB is adequately controlled, to minimize the risk of immune reconstitution inflammatory syndrome (IRIS). IRIS is a paradoxical worsening of symptoms that can occur in some PLWH after the initiation of ART, due to the restoration of immune function (10).

Pneumocystis pneumonia (PCP) is a severe life-threatening opportunistic infection that commonly affects HIV/AIDS patients with CD4 counts below 200 cells/mm³. The clinical presentation of PCP can be non specific, and the diagnosis is often based on clinical suspicion and radiographic findings and it is confirmed by BAL or induced sputum testing for Pneumocystis jirovecii. In our case, the patient was diagnosed with PCP based on clinical symptoms, CT and responded well to cotrimoxazole therapy and steroids.

Herpes genitalis is a common sexually transmitted infection (STI) in HIV-positive individuals. The presence of HIV can lead to more frequent and severe episodes of herpes, and the risk of viral shedding is also higher (11). Antiviral therapy with drugs such as acyclovir or valacyclovir is effective in controlling the symptoms and reducing the risk of transmission.

Vulvovaginal candidiasis is a common fungal infection that affects women of reproductive age. HIV infected women are at increased risk common in HIV-positive women, and recurrent episodes are common. The use of fluconazole is effective in treating candidiasis, but prolonged use can lead to the development of drug-resistant strains (12).

The existence of symbiotic relationship between these opportunistic infections is well established, where presence of one infection can lead to the development of another and together, they can significantly worsen the patient's condition. Early identification and prompt treatment of these infections are critical in improving patient outcomes. ART has been shown to reduce the risk of opportunistic infections in HIV/AIDS patients. In addition, prophylaxis for certain opportunistic infections is recommended in HIV/AIDS who have low

CD4 counts.

REFERENCES

1. Achhra AC, Petoumenos K, Law MG. Relationship between CD4 cell count and serious long-term complications among HIV-positive individuals. *Curr Opin HIV AIDS*. 2014 Jan;9(1):63-71. [PubMed]
2. Lawn SD, Harries AD, Williams BG, et al. Antiretroviral therapy and the control of HIV-associated tuberculosis. Will ART do it? *Int J Tuberc Lung Dis*. 2011;15(5):571-581.
3. Sterling TR, Pham PA, Chaisson RE. HIV infection-related tuberculosis: clinical manifestations and treatment. *Clin Infect Dis*. 2010;50 Suppl 3:S223-S230. doi:10.1086/651492
4. World Health Organization. Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. Geneva: World Health Organization; 2017. <https://www.who.int/publications/i/item/guidelines-for-managing-advanced-hiv-disease-and-rapid-initiation-of-antiretroviral-therapy>
5. Meintjes G, Lawn SD, Scano F, et al. Tuberculosis-associated immune reconstitution inflammatory syndrome: case definitions for use in resource-limited settings. *Lancet Infect Dis*. 2008;8(8):516-523. doi:10.1016/S1473-3099(08)70184-1
6. Kaur R, Kaur H, Mittal A. Herpes simplex virus type 2 infection: a risk factor for HIV infection. *Indian J Sex Transm Dis AIDS*. 2011;32(2):76-80. doi:10.4103/0253-7184.85412
7. Schacker T, Zeh J, Hu HL, Hill E, Corey L. Frequency of symptomatic and asymptomatic herpes simplex virus type 2 reactivations among human immunodeficiency virus-infected men. *J Infect Dis*. 1998;178(6):1616-1622. doi:10.1086/314502
8. Sobel JD, Chaim W. Treatment of *Torulopsis glabrata* vaginitis: retrospective review of boric acid therapy. *Clin Infect Dis*. 1997;24(4):649-652. doi:10.1093/clinids/24.4.649
9. Ai JW, Ruan QL, Liu QH, Zhang WH. Updates on the risk factors for latent tuberculosis reactivation and their managements. *Emerg Microbes Infect*. 2016 Feb 03;5(2):e10.
10. Lanzafame M, Vento S. Tuberculosis-immune reconstitution inflammatory syndrome. *J Clin Tuberc Other Mycobact Dis*. 2016 Mar 11;3:6-9. doi: 10.1016/j.jctube.2016.03.002. PMID: 31723680; PMCID: PMC6850228.
11. Abu-Raddad LJ, Magaret AS, Celum C, Wald A, Longini IM Jr, Self SG, Corey L. Genital herpes has played a more important role than any other sexually transmitted infection in driving HIV prevalence in Africa. *PLoS One*. 2008 May 21;3(5):e2230. doi: 10.1371/journal.pone.0002230. PMID: 18493617; PMCID: PMC2377333.
12. Scorzoni L, Fuchs BB, Junqueira JC, Mylonakis E. Current and promising pharmacotherapeutic options for candidiasis. *Expert Opin Pharmacother*. 2021 May;22(7):867-887. doi: 10.1080/14656566.2021.1873951. Epub 2021 Feb 4. PMID: 33538201; PMCID: PMC8122024.