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Case Report

Concurrent Cryptococcal Meningitis, Disseminated Histoplasmosis, and Tuberculosis Lymphadenitis in a Newly Diagnosed Human Immunodeficiency Virus Patient: An Unusual Case Report

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ABSTRACT

A 45-year-old male with a recent diagnosis of Human Immunodeficiency Virus (HIV) infection, initiated on antiretroviral therapy one month earlier, presented with a 15-day history of persistent headache, accompanied by vomiting for three days, cough, and significant weight loss over the past month. Physical examination revealed palpable left cervical lymphadenopathy. The patient had previously been hospitalized at another center, where he received treatment; however, evaluation for histoplasmosis had not been performed at that time. Fine-Needle Aspiration Cytology (FNAC) of the cervical lymph node demonstrated granulomatous lymphadenitis with the presence of *Histoplasma* species, confirming disseminated histoplasmosis. Due to persistent neurological symptoms, Cerebrospinal Fluid (CSF) examination was performed. India ink staining revealed numerous *Cryptococcus* organisms, while CSF parameters showed a glucose level of 28 mg/dL and protein level of 174 mg/dL, findings consistent with cryptococcal meningitis. The patient was started on amphotericin B and fluconazole, along with Antitubercular Therapy (ATT), levetiracetam for seizure prophylaxis, and supportive care. During treatment, amphotericin B-associated nephrotoxicity developed, with serum creatinine rising to 1.45 mg/dL. Consequently, amphotericin B was discontinued, and antifungal therapy was modified to flucytosine while continuing fluconazole and ATT. Following adjustment of the treatment regimen and supportive management, the patient showed gradual clinical improvement. This case describes a rare coexistence of cryptococcal meningitis, disseminated histoplasmosis, and tuberculous lymphadenitis in a newly diagnosed HIV patient. The report highlights the importance of early screening for multiple opportunistic infections, thorough diagnostic evaluation, and careful management of drug toxicities to improve outcomes in immunocompromised individuals.

Keywords: Cryptococcal meningitis, Histoplasmosis, HIV, Opportunistic infections, Tuberculosis.

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INTRODUCTION

Despite the widespread use of Antiretroviral Treatment (ART), opportunistic infections remain a major cause of morbidity and mortality in Human Immunodeficiency Virus (HIV) patients. Globally, cryptococcal meningitis accounts for almost 15% of Acquired Immunodeficiency Syndrome (AIDS) -related mortality, causing over 180,000 deaths per year (Perfect 2010; Rajasigham, 2017). Disseminated histoplasmosis affects about 5-10% of HIV patients in endemic places, whereas tuberculosis remains the most common co-infection, affecting up to one-third of HIV-infected people (Farooq 2020, Aguilar 2024). Tuberculosis is still one of the most prevalent life-threatening infections in advanced HIV patients (Perfect 2010; Jarwis 2022), whereas meningitis and histoplasmosis are less common but clinically significant co-infections (Rajasingham, 2017). The confluence of multiple illnesses in a single patient is extremely rare and poses diagnostic and treatment complications.

CASE PRESENTATION

A 45-year-old male who had been diagnosed with HIV infection one month earlier and recently initiated on Antiretroviral Therapy (ART) presented with a 15-day history of persistent headache, accompanied by vomiting for the past three days and associated cough. On clinical examination, enlargement of a left cervical lymph node was noted. Fine-Needle Aspiration

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Cytology (FNAC) of the lymph node revealed granulomatous lymphadenitis suggestive of tuberculosis (Figure 2), along with numerous intracellular yeast-like organisms morphologically consistent with *Histoplasma* species (Figures 1-4). The presence of *Histoplasma capsulatum* was confirmed using Periodic Acid-Schiff (PAS) and Gomori Methenamine Silver (GMS) staining (Figure 3). Considering the patient's persistent headache, further neurological evaluation was undertaken. Magnetic Resonance Imaging (MRI) of the brain demonstrated focal areas of leptomeningeal enhancement involving the right fronto-parietal lobes and interpeduncular cistern, suggestive of meningitis, along with an acute infarction in the right thalamo-capsular region (Table 1). A lumbar puncture was subsequently performed. Cerebrospinal Fluid (CSF) analysis showed a clear appearance with glucose of 28 mg/dL (serum glucose 96 mg/dL), protein of 174 mg/dL, and a total leukocyte count of 85 cells/mm^3 with lymphocytic predominance. India ink preparation and Cryptococcal Antigen (CrAg) testing were positive, demonstrating numerous encapsulated budding yeast cells consistent with *Cryptococcus neoformans*, confirming the diagnosis of cryptococcal meningitis. The patient was initially treated with intravenous amphotericin B deoxycholate (0.7 mg/kg/day) in combination with fluconazole 400 mg/day. Concurrent antitubercular therapy was initiated with isoniazid 75 mg, rifampicin 150 mg, pyrazinamide 400 mg, and ethambutol 275 mg (three tablets daily). During the course of treatment, the patient's serum creatinine increased to 1.45 mg/dL, prompting modification of the antifungal regimen to oral flucytosine (500 mg; 3-2-2-2 dosing schedule). Levetiracetam was also initiated for seizure prophylaxis. In addition, supportive management, including adequate hydration, antipyretics, and nutritional supplementation, was provided.

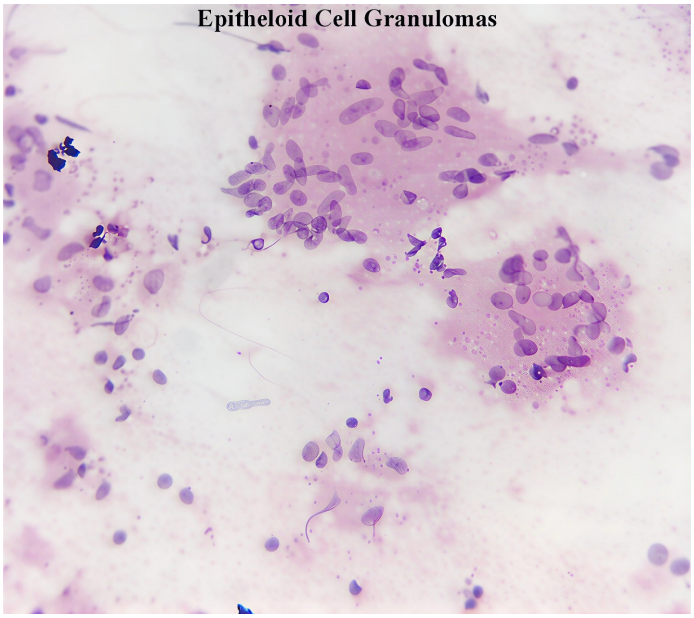

Figure 1: Photomicrograph of fine-needle aspiration cytology (FNAC) from the cervical lymph node showing well-formed epithelioid cell granulomas, suggestive of granulomatous lymphadenitis consistent with a tuberculous aetiology.

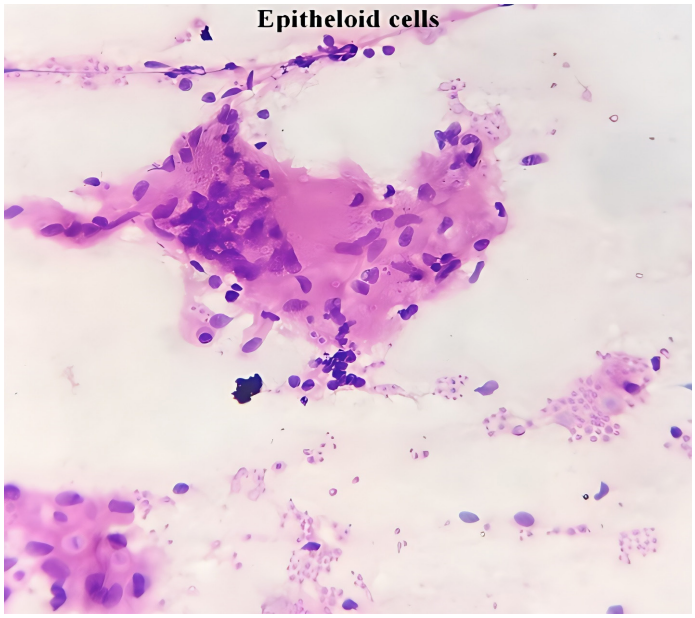

Figure 2: Cytological smear demonstrating clusters of epithelioid cells with elongated nuclei and pale cytoplasm, representing activated macrophages typically seen in granulomatous inflammation.

Table 1: **Flow cytometry-based lymphocyte subset analysis report.**

	Observed value	Units	Normal value
CD4	15	Cells/mm^3	500-1500
% CD3+ / CD45 (T-cells)	84.71↑	%	59.43 - 84.36
% CD3+ / CD4+ (T-Helper cells)	2.2↓	%	27.9 - 50.5
%CD3+ /CD8+ (T-Suppressor cells)	81.64↑	%	18.47 - 40.83
Absolute CD3 + T Lymphocytes count	594.67↓	Cell/c.mm	1007 - 2479
Absolute CD4 + T Helper cells count	15.41↓	Cells/c.mm	371 - 1217
Absolute CD8 + T suppressor cell count	573.09	Cells/c.mm	355 - 1171
Ratio CD4 / CD8	0.03↓	Ratio	0.72 - 2.10

CD3: Cluster of differentiation 3, CD4: Cluster of differentiation 4, T Lymphocytes: Thymus - derived lymphocytes

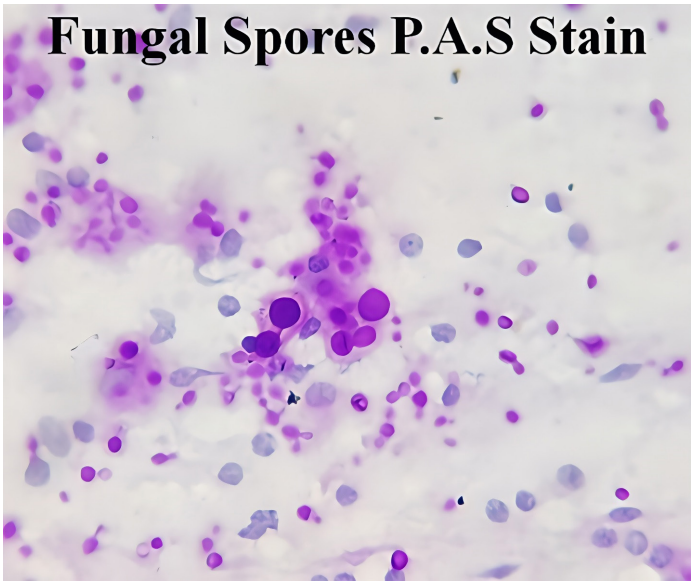

Figure 3: Periodic acid-Schiff (PAS) stained smear highlighting numerous fungal spores appearing as magenta-colored, round to oval yeast-like structures, consistent with *Histoplasma* species.

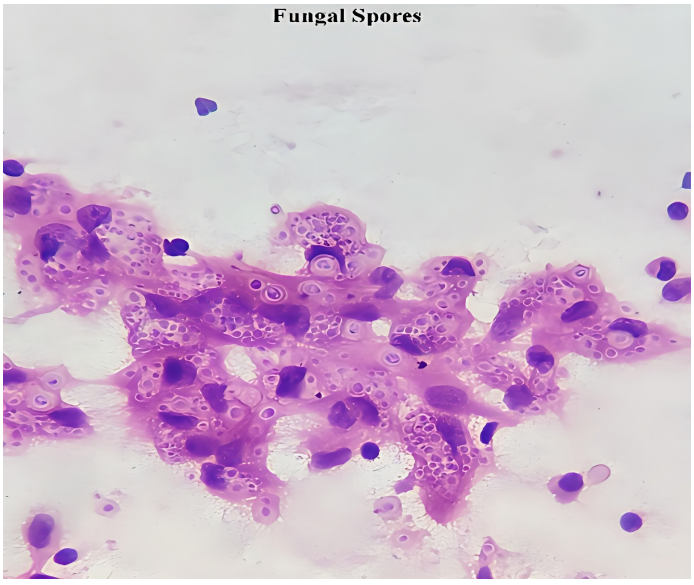

Figure 4: High-power view showing multiple intracellular and extracellular fungal spores within macrophages, morphologically suggestive of *Histoplasma capsulatum*.

Table 2: Diagnostic workup.

Test Name	Result
A.F.B. Stain	A.F.B. not found
CSF CBNAAT	Not detected
HBsAg	Negative
MRI Brain	Focal areas of leptomeningeal enhancement along the right fronto-parietal lobes and inter-peduncular cistern - likely changes of meningitis Acute infarction right thalamo-capsular region

AFB stain: Acid-fast bacillus, CSF CBNAAT: Cerebrospinal fluid Cartridge-Based Nucleic Acid Amplification Test, HBsAg: Hepatitis B Surface Antigen, MRI: Magnetic Resonance Imaging

DISCUSSION

Opportunistic Infections (OIs) remain a significant cause of illness and death among people living with HIV, especially in individuals with advanced immunosuppression (WHO 2022). The occurrence of multiple opportunistic infections in a single patient is uncommon, and the simultaneous presence of three infections presents considerable diagnostic and therapeutic challenges (Farooq 2020; Gonzalez 2015). HIV infection leads to progressive depletion of CD4+ T lymphocytes, resulting in impaired cell-mediated immunity (Table 2). This immunological dysfunction increases susceptibility to several opportunistic pathogens, particularly fungal and mycobacterial infections (Perfect 2010). The clinical manifestations of these infections often overlap, with symptoms such as fever, weight loss, lymphadenopathy, and neurological involvement, which can complicate early diagnosis. In the present case, Fine-Needle Aspiration Cytology (FNAC) of a cervical lymph node confirmed tuberculous lymphadenitis and revealed the presence of *Histoplasma* species. Additionally, Cerebrospinal Fluid (CSF) examination demonstrated findings consistent with cryptococcal meningitis, while microbiological investigations further supported the diagnosis of tuberculosis.

Management of multiple concurrent opportunistic infections requires careful therapeutic planning. Amphotericin B is commonly used for the treatment of cryptococcosis and disseminated histoplasmosis; however, its use may be limited by adverse effects such as nephrotoxicity. In our patient, an increase in serum creatinine to 1.45 mg/dL was observed, necessitating modification of antifungal therapy to flucytosine. The timing of Antiretroviral Therapy (ART) initiation is also critical, as inappropriate timing may increase the risk of immune reconstitution inflammatory syndrome (IRIS). Furthermore, amphotericin B-associated nephrotoxicity is relatively common and requires close monitoring of renal function and electrolyte levels during treatment. Early recognition of opportunistic infections, along with prompt initiation of appropriate therapy and supportive care, is essential for improving patient outcomes. Although reports describing dual or triple opportunistic infections in individuals with HIV are rare, this case highlights the importance of maintaining a high level of clinical suspicion, particularly in regions where these infections are endemic (Medina 2021; Aguilar 2024).

CONCLUSION

The simultaneous occurrence of cryptococcal meningitis, histoplasmosis, and tuberculosis in a patient with HIV is extremely rare. This case underscores the need for clinicians to maintain a high index of suspicion when evaluating immunocompromised individuals presenting with non-specific symptoms. A comprehensive diagnostic approach is essential to accurately identify coexisting opportunistic infections. In addition, treatment strategies should be individualized, taking into account the complexity of managing multiple infections and the potential for drug-related toxicities. Early diagnosis, prompt initiation of appropriate therapy, and close monitoring during treatment are a must for improving clinical outcomes in patients with advanced immunosuppression.

ACKNOWLEDGEMENT

None.

ABBREVIATIONS

HIV: Human Immunodeficiency Virus; **ART:** Antiretroviral therapy; **FNAC:** Fine-Needle Aspiration Cytology; **CSF:** Cerebrospinal fluid; **ATT:** Antitubercular therapy; **AIDS:** Acquired Immunodeficiency Syndrome; **PAS:** Periodic Acid-Schiff; **GMS:** Gomori methenamine silver; **MRI:** Magnetic Resonance Imaging; **CrAg:** Cryptococcal antigen; **OIs:** Opportunistic infections; **IRIS:** Immune reconstitution inflammatory syndrome; **CD4:** Cluster of differentiation 4; **CD3:** Cluster of differentiation 3; **CD8:** Cluster of differentiation 8; **AFB:** Acid-fast bacillus; **CBNAAT:** Cartridge-Based Nucleic Acid Amplification Test; **HBsAg:** Hepatitis B Surface Antigen.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

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PATIENT PERSPECTIVE

I had been feeling unwell for weeks and did not know the cause. After the diagnosis, I was relieved to receive correct treatment. Though the medicines were strong and caused side effects, I felt better each week. I am grateful that the doctors continued to monitor me and adjust the treatment.

INFORMED CONSENT

Written informed consent for publication of this case report and accompanying images was obtained from the patient.

AUTHOR STATEMENT

We declare that this manuscript, entitled "Concurrent Cryptococcal Meningitis, Disseminated Histoplasmosis, and Tuberculosis Lymphadenitis in a Newly Diagnosed HIV Patient: An Unusual Case Report," is original and has not been published before. All authors have approved the manuscript and agree with its submission to "Journal of Pharmacy Practice and Community Medicine". We further confirm that the order of authors listed in the manuscript has been approved by all of us. We understand that the Corresponding Author is the sole contact for the Editorial process.

REFERENCES

Aguilar, G., Cáceres, D. H., Samayoa, B., Medina, N., Lau-Bonilla, D., Mercado, D. *et al.* (2024). Implementation of a rapid diagnostic assay package for histoplasmosis, cryptococcosis, and tuberculosis in people with advanced HIV disease. BMC Infectious Diseases, 24(1), Article 707.

Farooq, H. Z., Hannan, A., Jaffar, N., Hussain, T., Waheed, Y., & Saeed, U. (2020). Disseminated histoplasmosis complicated by concurrent cryptococcal meningitis in an HIV-positive patient: A case report. IDCases, 19, Article e00723.

González, G. M., Esquivel, J., Ayala, J., & Figueroa, J. I. (2015). Multiple opportunistic fungal infections in an individual with advanced AIDS. Revista Iberoamericana de Micologia, 32(2), 129–132.

Jarvis, J. N., Lawrence, D. S., Meya, D. B., Kagimu, E., Kasibante, J., Mpoza, E., Rutakingirwa, M. K., Ssebambulidde, K., Tugume, L., Rhein, J., Boulware, D. R., Mwandumba, H. C., Moyo, M., Mzinganjira, H., Kanyama, C., Hosseinipour, M. C., Chawinga, C., Meintjes, G., Schutz, C., . . . Ambition Study Group. (2022). Single-dose liposomal amphotericin B treatment for cryptococcal meningitis. The New England Journal of Medicine, 386(12), 1109–1120. https://doi.org/10.1056/NEJMoa2111904

Medina, N., Alastruey-Izquierdo, A., Bonilla, O., Gamboa, O., Mercado, D., Pérez, J. C., Salazar, L. R., Arathoon, E., Denning, D. W., & Rodriguez-Tudela, J. L. (2021). A rapid screening program for histoplasmosis, tuberculosis, and cryptococcosis reduces mortality in HIV patients from Guatemala. Journal of Fungi, 7(4), Article 268. https://doi.org/10.3390/jof7040268

Perfect, J. R., Dismukes, W. E., Dromer, F., Goldman, D. L., Graybill, J. R., Hamill, R. J., Harrison, T. S., Larsen, R. A., Lortholary, O., Nguyen, M.-H., Pappas, P. G., Powderly, W. G., Singh, N., Sobel, J. D., & Sorrell, T. C. (2010). Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. Clinical Infectious Diseases, 50(3), 291–322. https://doi.org/10.1086/649858

Rajasingham, R., Smith, R. M., Park, B. J., Jarvis, J. N., Govender, N. P., Chiller, T. M., Denning, D. W., Loyse, A., & Boulware, D. R. (2017). Global burden of disease of HIV-associated cryptococcal meningitis: An updated analysis. The Lancet. Infectious Diseases, 17(8), 873–881. https://doi.org/10.1016/S1473-3099(17)30243-8

Vechi, H. T., Chaves, G. M., Freitas, R. S., Costa, F., da Silva, D., & Oliveira, R. C. (2019). Invasive fungal infection by Cryptococcus neoformans var. grubii in HIV/AIDS patients: Clinical features, treatment, and outcomes. BMC Infectious Diseases, 19(1), Article 893.

World Health Organization. (2022a). Recommendations on induction, consolidation and maintenance therapy for cryptococcal disease in HIV. World Health Organization. https://www.ncbi.nlm.nih.gov/books/NBK581839/

World Health Organization. (2022b). Guidelines for diagnosing, preventing and managing cryptococcal disease. WHO. https://www.who.int/publications/i/item/9789240052178

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