

Unmasking IRIS in Advanced HIV: Disseminated Histoplasmosis Following HAART in a Case of Smear-Negative Tuberculosis Complicated with Septic Shock and Iatrogenic Pneumothorax

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INTRODUCTION

Advanced HIV (retroviral disease, RVD) is usually associated with opportunistic infections, especially in patients with profound immunosuppression. Highly Active Antiretroviral Therapy (HAART) has improved clinical and immunological outcomes for people living with HIV.

However, the initiation of HAART can also trigger a complex inflammatory condition known as Immune Reconstitution Inflammatory Syndrome (IRIS), a complex inflammatory response that can unmask or worsen underlying infections. The complex interplay between advanced human immunodeficiency virus infection, opportunistic infections, and immune reconstitution inflammatory syndrome further complicates patient management.

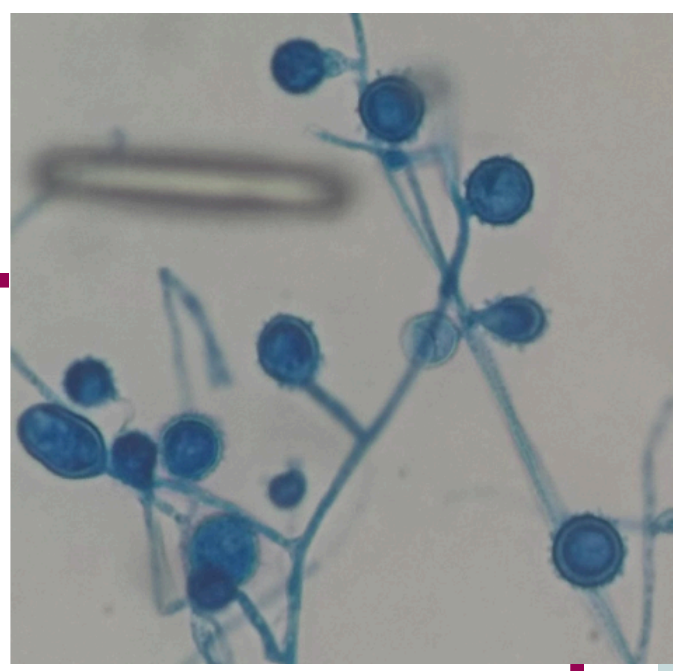
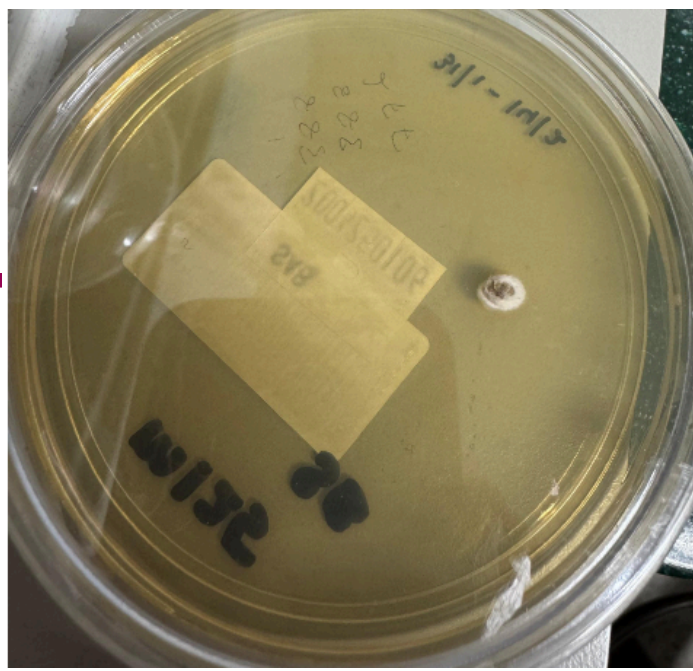


Figure 1: Sabouraud dextrose agar culture at 25°C showing small, white, cotton-like colonies of *Histoplasma capsulatum* on Day 9.

Figure 2: Hyaline and septate hyphae with abundant tuberculate, thick-walled macroconidia (Lactophenol cotton blue stain x40)

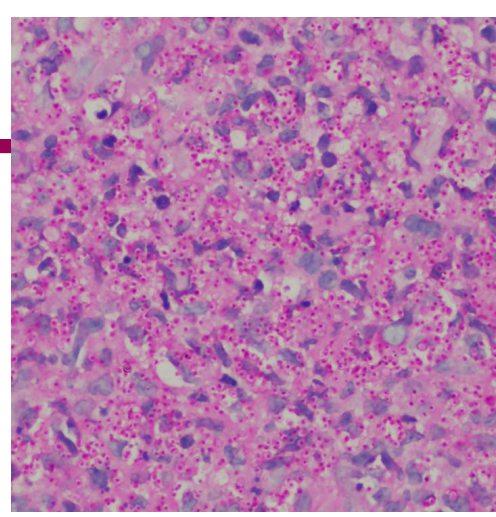
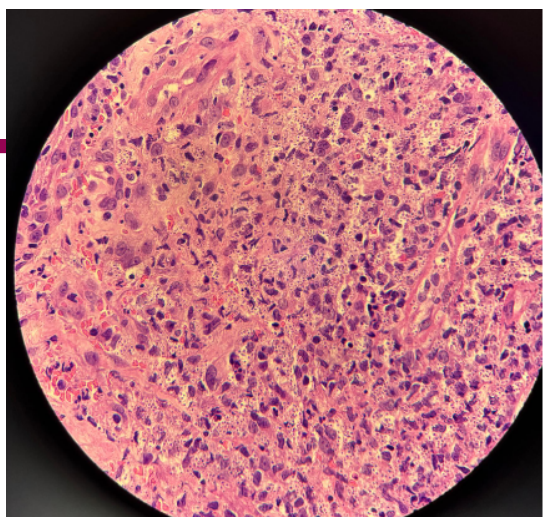


Figure 3: Tissue biopsy showed dense inflammation with intracytoplasmic fungal bodies with clear pale halo as highlighted with periodic acid Schiff stain

CONCLUSION

This case serves as an important reminder of the potential for unmasking immune reconstitution inflammatory syndrome (IRIS) to develop in patients with advanced HIV, even in the presence of severe opportunistic infections like tuberculosis (TB). This case report underscores the important key takeaways, including the early recognition of IRIS, the need for proactive diagnostic workups, and the importance of effective multidisciplinary management and supportive care to ensure promising patient outcomes.

CASE REPORT

A 47-year-old man with newly diagnosed advanced HIV initially presented with generalised lethargy and fever for 1 week, with a history of prolonged cough. On examination, he was tachycardic, febrile and had oral candidiasis. Chest x-ray upon arrival noted a cavitation lesion of both upper lobes. The HIV rapid test was reactive; urine TB LAM was positive with a negative AFB smear. Further laboratory investigation showed seropositive syphilis infection, CD4 level of 0 cells/ μ L, with high HIV-1 viral load. He was then treated with anti-tuberculous treatment and benzathine penicillin prior to initiation of HAART.

Following HAART initiation, he then presented with generalised body rash and hematochezia. Further laboratory investigation reveals that the patient developed disseminated histoplasmosis, consistent with unmasking immune reconstitution inflammatory syndrome (IRIS) as detected by positive blood and tissue fungal cultures, confirmed by internal transcribed spacer (ITS) sequencing done at Institute Medical Research (IMR), supported by histopathological findings from skin and rectal biopsies.

He was then treated with liposomal amphotericin B; however complicated by hospital-acquired infection and septic shock, along with iatrogenic pneumothorax requiring intensive care and broad-spectrum antibiotics. Antiretroviral therapy was resumed after stabilisation, and he was eventually discharged in a stable condition.

DISCUSSION

This case illustrates the challenges of managing advanced HIV cases. The patient was in a severe immunosuppression state as evidenced by a CD4 count of 0 cells/ μ L with high HIV-1 viral load, which increases their susceptibility to opportunistic infection (Calmy et al., 2018). The initial presentation of pulmonary tuberculosis (TB) is a common opportunistic infection mainly in immunocompromised individuals in Malaysia (Fadzil et al., 2025). This diagnosis was supported by chest x-ray findings with positive urine TB LAM test, despite a negative sputum smear. This finding highlights the limitations of conventional AFB microscopy in immunocompromised patients, due to its low sensitivity, which further complicates diagnosis, especially in resource-limited settings (Kumar et al., 2023; Matee et al., 2008).

The patient's initial management, with anti-tuberculous treatment and syphilis therapy before HAART initiation, is important as it needs to prevent and manage IRIS, minimise complications, and ensure the most favourable treatment outcomes.

However, after the HAART initiation, the patient's condition turned into a critical point due to the development of disseminated histoplasmosis as an unmasking IRIS, due to immunological paradoxes inherent in immune recovery, where a reconstituted immune response can lead to an exacerbation of inflammatory response against the dormant pathogens (Kaplan et al., 2023). The diagnostic finding of positive fungal cultures confirmed ITS sequencing, and histopathological findings from skin and rectal biopsies highlight the role of laboratory diagnosis in aiding the detection and management of IRIS.

The patient unfortunately deteriorated and developed septic shock, a life-threatening systemic infection, as well as an iatrogenic pneumothorax, which is a collapsed lung caused by a medical procedure due to positive pressure ventilation. These complications highlight the extreme vulnerability of patients with advanced HIV, particularly when they are undergoing intensive treatment, emphasising the need for critical care support.

This successful management of this challenging case emphasises the importance of a multidisciplinary team approach, which led to favourable outcomes for the patient.