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### Late Onset Immune Reconstitution Inflammatory Syndrome presenting as Infectious Meningitis

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## Introduction

Immune reconstitution inflammatory syndrome (IRIS) refers to a paradoxical worsening of a preexisting infectious disease or the unmasking of an occult infectious disease after initiation of antiretroviral therapy (ART). Table 1 summarizes the diagnostic criteria (1–5). IRIS is a diagnosis of exclusion and should only be made after other etiologies have been ruled out, which can involve a thorough imaging and microbial workup.

IRIS has been associated with a diverse multitude of infectious agents that comprise bacterial, fungal, and viral pathogens. These include but are not limited to *Mycobacterium tuberculosis*, *Mycobacterium avium complex*, *Cryptococcus neoformans*, *Pneumocystis jirovecii*, CMV, Herpes simplex, Hepatitis B, and HHV8. Symptoms of IRIS can vary depending on the organism involved. However, they are generally consistent with an inflammatory process and can include fever, fatigue, night sweats, nausea, weight loss, and shortness of breath. For IRIS presenting after cryptococcal meningitis, symptoms resemble those of meningitis, such as nausea, headache, eye pain, photophobia, and nuchal rigidity (6,7). Typically, IRIS occurs within the first few months after initiation of ART.

## Objective

We report a case of immune reconstitution inflammatory syndrome (IRIS) occurring 8 months after ART initiation presenting with symptoms resembling recurrence of his *cryptococcal meningitis*.

## IRIS Diagnosis

AIDS with Low Pretreatment CD4<sup>1</sup>

(+) ART Response<sup>2</sup>

New or Worsening Symptoms<sup>3</sup> after ART

Unexplained<sup>4</sup> Symptoms

Temporal Relationship between ART and Symptoms

**Table 1. IRIS Diagnostic Criteria**

<sup>1</sup>Exception: *Mycobacterium tuberculosis*

<sup>2</sup>Decreased viral load by >1 log copies/mL, increased CD4 count

<sup>3</sup>Symptoms of an infection or inflammatory condition

<sup>4</sup>Not explained by new/previously diagnosed infection, drug therapy effects, or patient non-compliance

## Case Report

A 35-year-old African American male presented 9 months after diagnosis of cryptococcal meningitis, for which he remained on maintenance therapy with fluconazole after he had completed induction therapy with Ambisome and consolidation therapy.

It had been **8 months since the initiation of ART** when he presented to the emergency department with headache, photophobia, ataxia, and gait instability. The patient reported adherence to **ARTs and fluconazole**, and recent labs revealed an **undetectable HIV viral load and a CD4 count of 143** (improved from 4). MRI of the brain revealed diffuse leptomeningeal enhancement consistent with cryptococcal meningitis. Lumbar puncture revealed an **opening pressure of 44**, WBC 56, protein 56, glucose 22, and positive cryptococcal antigen (1:160 titer). He was restarted on induction therapy with AmBisome and flucytosine due to concern for cryptococcal meningitis recurrence, and serial lumbar punctures were performed with persistently elevated opening pressures. Blood cultures and multiple CSF cultures had no growth throughout the hospital admission. Due to **persistent negative cultures**, the patient was now thought to have immune reconstitution inflammatory syndrome (**IRIS**). He was started on **prednisone**, and **serial lumbar punctures** were continued to reduce intracranial pressure (Table 2). The last opening pressure was 20, and the patient was discharged on a prednisone taper.

## Results

Lumbar Puncture #	Opening Pressure (mmHg)
1	44
2	45
3	>60
4	46
5	39
6	33
7	30
8	26
9	27
10	27
11	23
12	20

**Table 2. Serial Lumbar Punctures and Opening Pressures**

## Conclusion

This case illustrates the importance of considering IRIS in patients who have undergone treatment for disseminated cryptococcus or cryptococcal meningitis and initiation of antiretroviral therapy, even beyond the classic timeframe. Furthermore, if IRIS is on the differential, following the CSF cultures is crucial to help distinguish IRIS from recurrence of cryptococcal meningitis.

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