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Case Report

Paradoxical Immune Reconstitution Inflammatory Syndrome Presenting as Pulmonary KOCHs: A Rare Case.

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ABSTRACT

Immune reconstitution inflammatory syndrome (IRIS) is a well-recognized complication in patients with advanced human immunodeficiency virus (HIV) infection following the initiation of antiretroviral therapy (ART). The quick restoration of immunological function causes an increased inflammatory response to opportunistic infections. The most frequent illness linked to IRIS is tuberculosis (TB), especially in those with severe immunosuppression. TB-associated IRIS can show up as the unmasking of an infection that was previously undiagnosed or as a paradoxical worsening of tuberculosis. We report the case of a 58-year-old female diagnosed with HIV-1 and HIV-2 infection with severe immunosuppression (CD4 count 28 cells/µL). No previous history of tuberculosis. After 3 week of ART initiation, the patient developed severe breathlessness, cough, fever, and loss of appetite. Clinical examination revealed tachycardia, pallor, and respiratory findings including rhonchi and harsh conducted breath sounds. Repeat CD4 count increased to 98 cells/µL, indicating immune recovery. High-resolution computed tomography (CT) of the chest revealed diffuse bilateral centrilobular nodules with a tree-in-bud appearance, patchy ground-glass opacities, and mediastinal lymphadenopathy suggestive of pulmonary tuberculosis. The patient was diagnosed with pulmonary tuberculosis likely representing unmasking tuberculosis-associated IRIS and was started on standard anti-tubercular therapy (ATT) with isoniazid, rifampicin, pyrazinamide, and ethambutol. Supportive management including correction of anemia was provided. The patient showed gradual clinical improvement with treatment and highlights the importance of early recognition of TB-associated IRIS following ART initiation in severely immunocompromised HIV patients and emphasizes the need for prompt diagnosis and management.

Keywords: *HIV, Tuberculosis, Immune Reconstitution Inflammatory Syndrome, ART, Pulmonary Koch's Disease.*

INTRODUCTION

One of the most deadly infectious illnesses in the world is still tuberculosis (TB). Global estimates indicate that almost 10.7 million people infected tuberculosis, and in 2025 and over 1.2 million deaths in 2024 [1]. The prevalence of HIV-TB coinfection varies greatly throughout the world, from about 3% in some parts of the world to as high as 65–72% in high-burden environments. Since TB infection leads to increases in HIV replication and HIV infection contributes to TB progression secondary to immunosuppression, it should come as no surprise that TB burden remains highest in areas of the world that hold the highest HIV prevalence [2,3]. Due to high HIV incidence, a lack of healthcare resources, and socioeconomic difficulties, low- and middle-income nations especially those in sub-Saharan Africa bear the brunt of this dual epidemic [3]. TB-IRIS prevalence rates as high as 20-30% in HIV-positive individuals, while the presence of IRIS in similarly immunocompromised HIV-positive individuals is currently unknown [4].

In 2006, the International Network for the Study of HIV-associated Immune Reconstitution Inflammatory Syndrome (INSHI) proposed standardized case definitions for two major forms of tuberculosis-associated IRIS: **paradoxical TB-IRIS** and **unmasking TB-IRIS**. Paradoxical TB-IRIS is characterized by the clinical or radiological deterioration of

previously diagnosed tuberculosis after the initiation of highly active antiretroviral therapy (HAART), despite the patient receiving appropriate anti-tubercular treatment (ATT) [5,6]. This condition differs from a tuberculosis paradoxical reaction that may occur after the initiation of ATT and is not related to immune recovery; therefore, it can also be observed in individuals without HIV infection. Paradoxical TB-IRIS typically occurs in patients with active or latent tuberculosis who begin HAART and subsequently develop worsening inflammatory manifestations [7].

A paradoxical reaction to tuberculosis may occur following the initiation of anti-tubercular therapy (ATT), but unlike TB-IRIS, it is not associated with immune restoration and may be observed in patients irrespective of their HIV status.

CASE PRESENTATION:

A 58-year-old female presented to the hospital with a diagnosis of HIV-1 and HIV-2 infection and was admitted to the Department of Medicine for further evaluation and management. There was no history of tuberculosis, asthma, ischemic heart disease (IHD), diabetes mellitus, or hypertension.
Baseline immunological assessment revealed a CD4 count of 28 cells/µL, indicating severe immunosuppression.

Clinical Examination:
On physical examination, the patient's general condition was good and she was hemodynamically stable.

Vital signs were as follows:

- Pulse Rate: 88/min
- Respiratory Rate: 16 cycles per minute.
- Blood Pressure: 120/80 mmHg.
- Oxygen Saturation (SpO_2): 99%

Systemic Examination:
Cardiovascular System (CVS): First and second heart sounds (S1, S2) were normal. No murmurs were heard.

Respiratory System (RS): Breath sounds were bilaterally equal with no added sounds.
Based on her immunological status, the patient was started on antiretroviral therapy (ART) consisting of: Tenofovir 300 mg, Lamivudine 300 mg and Dolutegravir 50 mg**.**

Clinical Course after ART Initiation:
Approximately 3 weeks after initiation of ART, on examination patient complained severe breathlessness, Persistent cough, Fever and Loss of appetite.
These symptoms were suggestive of an acute inflammatory or infectious process.

Clinical Examination during Symptomatic Phase
On examination, the following findings were noted:
Vital Signs : Pulse Rate: **110/min**, Blood Pressure: **110/78 mmHg**, Respiratory Rate: **20 cycles per minute** and Oxygen Saturation: **94% on room air. Pallor ++ present**
There were no signs of congestive cardiac failure (CCF). Tachycardia present and Heart sounds otherwise normal.

Respiratory System: Ronchi present and Harsh conducted breath sounds noted bilaterally

Laboratory Investigations: The patient was admitted for further evaluation, and laboratory investigations were performed. Hemoglobin (Hb): 8.9 g/dL**,** Total Leukocyte Count (TLC): 19,190 cells/mm³, CRP>26mg/dl, ESR: 54mm/hr, Viral load : less than 5.3 log 10 copies/ml, CD4: 28 cells/micro litre and Other routine laboratory parameters were within normal limits.

After 2 months of intensive phase CD4: 98 cells/micro litre, Viral load : 5.5 log 10 copies/ml
After 6 months A **repeat CD4 count showed improvement to 550 cells/µL,** Viral load: 2.0 log 10 copies/ml indicating immune recovery after initiation of ART

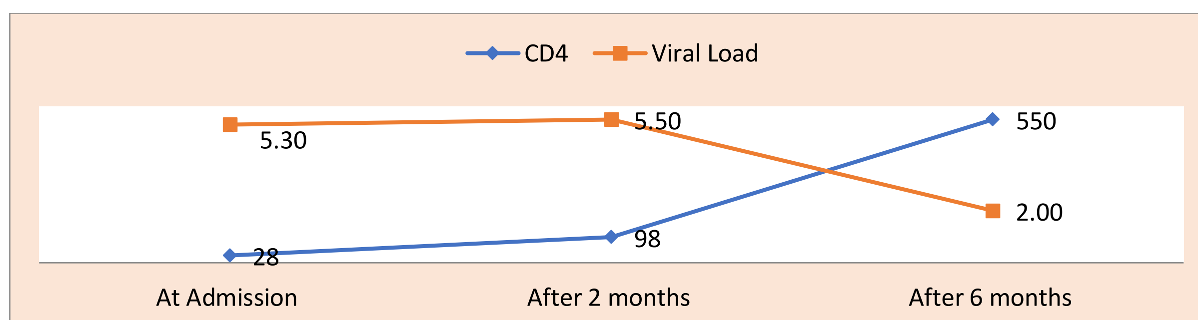

Figure 1: CD4 & Viral Load at Admission, after 2 months and after 6 months of after initiation of treatment.

Radiological Findings:

A CT scan of the chest was performed to evaluate the respiratory symptoms. Diffuse bilateral centrilobular nodules with tree-in-bud appearance. Areas of patchy ground- glass opacifications / mosaic attenuation in bilateral lungs. Few marginally enlarged mediastinal lymph nodes & prominent bilateral axillary lymph nodes. In an immunocompromised host, these radiological findings were highly suggestive of acute endobronchial infection, most likely pulmonary tuberculosis.

Diagnosis: Based on the clinical presentation, radiological findings, severe baseline immunosuppression, and temporal association with ART initiation, a diagnosis of pulmonary tuberculosis likely representing unmasking tuberculosis-associated immune reconstitution inflammatory syndrome (TB-IRIS) was made.

Management: The patient was started on standard anti-tubercular therapy (ATT) for pulmonary tuberculosis. Also Oral hematinic added for HB correction.

Intensive Phase (2 months): Isoniazid (H) – 5 mg/kg, Rifampicin (R) – 10 mg/kg, Pyrazinamide (Z) – 25 mg/kg, Ethambutol (E) – 15 mg/kg.
This was planned to be followed by a continuation phase of 4 months with HRE regimen.

Supportive management included: Correction of anemia, Nutritional support and Continuation of antiretroviral therapy.

Outcome and Follow-Up: Following initiation of anti-tubercular therapy and supportive treatment, the patient showed gradual clinical improvement. Her respiratory symptoms improved, and general condition stabilized. She continues to be monitored for response to treatment and adherence to ART and ATT.

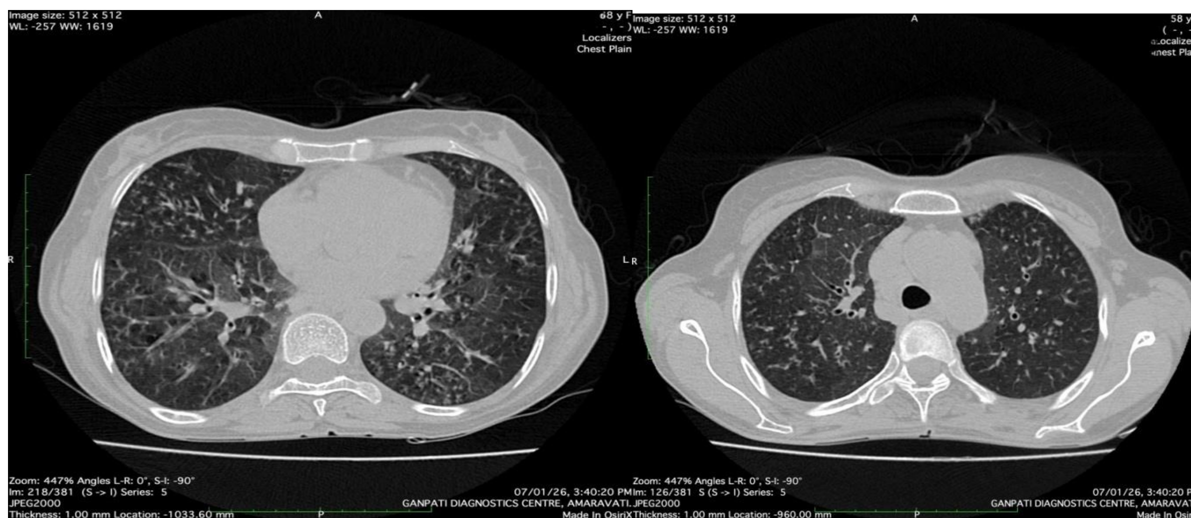

Figure:2 *Figure: 3*

Figure 2: Axial CT Chest Showing Diffuse Bilateral Centrilobular Nodules with Tree-in-Bud Appearance.
Figure 3: Axial CT Chest Showing Diffuse Bilateral Centrilobular Nodules with Tree-in-Bud Pattern and Patchy Ground-Glass Opacities

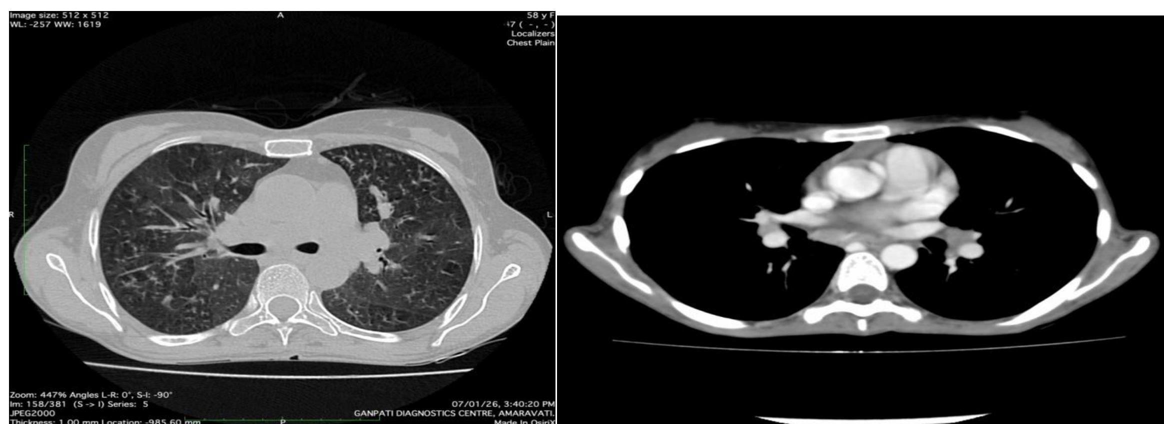

Figure:4 *Figure: 5*

Figure 4: Axial CT Chest Demonstrating Diffuse Tree-in-Bud Nodularity and Ground-Glass Opacities.
Figure 5: Axial CT Chest Demonstrating Mediastinal and Hilar Lymphadenopathy Suggestive of Tuberculous Involvement in an HIV-Infected Patient.

DISCUSSION:

TB-associated IRIS represents one of the most frequent complications encountered after the initiation of antiretroviral therapy in patients with advanced HIV infection. The condition results from restoration of immune responses against mycobacterial antigens leading to an exaggerated inflammatory reaction. Patients with **severely reduced CD4 counts (<50 cells/µL)** are at highest risk of developing IRIS. In the present case, the baseline CD4 count was **28 cells/µL**, placing the patient in a high-risk category. The rapid increase in CD4 count following ART initiation reflects immune recovery. In this case, the CD4 count increased to **98 cells/µL**, indicating immune reconstitution. Shang W etal [8] found CD4 count of 122 cells/µL, in combination with a corresponding high viral load, placed her at high risk for IRIS.

IRIS has a heterogeneous presentation and can be difficult to diagnose. The following conditions can closely mimic IRIS and must be considered or excluded before the diagnosis of IRIS is made. Alternative conditions may include: (1) non-adherence to medication, (2) medication side effects, (3) infection not yet diagnosed, and even (4) malignancy.
Radiological findings in TB-IRIS commonly include: Tree-in-bud nodules, Centrilobular nodules, Ground-glass opacities and Lymphadenopathy.

The management of TB-IRIS involves continuation of ART alongside appropriate anti-tubercular therapy. Discontinuation of ART is generally avoided except in life-threatening situations. Corticosteroids may be considered in severe inflammatory reactions.

Early recognition is essential because TB-IRIS may be misdiagnosed as treatment failure or drug resistance.

CONCLUSION:

In patients with advanced HIV infection, immune reconstitution inflammatory syndrome is a side effect that occurs after antiretroviral medication is started. One of the most prevalent types of IRIS, especially in patients with extremely low baseline CD4 levels, is still tuberculosis-associated IRIS. This particular case emphasizes how crucial it is to keep a high index of suspicion for tuberculosis in HIV patients who experience new respiratory symptoms soon after beginning antiretroviral therapy. Improving results requires prompt anti-tubercular therapy beginning and early diagnosis.

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