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REPORTE DE CASO

IRIS-associated large Tuberculous Lymphadenitis in an HIV-Positive Patient

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Abstract

We present the case of a 53-year-old woman with longstanding HIV infection who experienced severe immunosuppression after discontinuing antiretroviral therapy (ART), later restarting ART with successful viral suppression and immune recovery. She subsequently developed pulmonary tuberculosis with acute respiratory distress syndrome and bronchogenic dissemination, which was confirmed to be sensitive to first-line drugs. Following another discontinuation and resumption of both anti-tuberculous therapy and ART, the patient developed extensive bilateral cervical lymphadenopathy with fistulous tracts. Imaging revealed enormous necrotic lymph nodes, and percutaneous ultrasound-guided drainage produced purulent fluid that was sterile for *Mycobacterium tuberculosis*, including by PCR. This presentation of large, necrotic, suppurative lymphadenopathy as part of immune reconstitution inflammatory syndrome (IRIS)is rare and diagnostically challenging. The case highlights the clinical complexity of IRIS in HIV-tuberculosis co-infection and underlines the value of imaging and multidisciplinary care. Early recognition of IRIS allows for the continuation of ART and tuberculosis therapy, while targeted management of inflammatory complications is essential. This report emphasizes the potential for unusually severe lymph node involvement in IRIS and the importance of adherence to both ART and TB treatment for optimal patient outcomes.

Keywords: HIV Infections; Tuberculosis Lymph Node; Immune Reconstitution Inflammatory Syndrome; Lymphadenopathy; Antiretroviral Therapy

Linfadenitis tuberculosa extensa asociada a IRIS en un paciente con VIH

Resumen

Presentamos el caso de una mujer de 53 años con infección por VIH de larga evolución que experimentó una inmunosupresión grave tras interrumpir el tratamiento antirretroviral (TAR), reiniciando posteriormente el TAR con supresión viral e inmunológica exitosa. Posteriormente desarrolló tuberculosis pulmonar con síndrome de distrés respiratorio agudo y diseminación broncogénica, confirmada como sensible a los fármacos de primera línea. Tras una nueva interrupción y reanudación tanto del tratamiento antituberculoso como del TAR, la paciente presentó una linfadenopatía cervical bilateral extensa con trayectos fistulosos. Las pruebas de imagen revelaron ganglios linfáticos necrosados de gran tamaño, y el drenaje percutáneo guiado por ecografía produjo un líquido purulento estéril para *Mycobacterium tuberculosis*, incluida la PCR. Esta presentación —linfadenopatía grande, necrótica y supurativa como parte del síndrome inflamatorio de reconstitución inmunitaria (IRIS)— es infrecuente y plantea un desafío diagnóstico. El caso resalta la complejidad clínica del IRIS en la coinfección VIH-tuberculosis y subraya el valor de la imagenología y la atención multidisciplinaria. El reconocimiento precoz del IRIS permite la continuación del TAR y del tratamiento antituberculoso, mientras que el manejo dirigido de las complicaciones inflamatorias es esencial. Este informe enfatiza el potencial de una afectación ganglionar inusualmente grave en el IRIS y la importancia de la adherencia tanto al TAR como al tratamiento antituberculoso para lograr resultados óptimos en los pacientes.

Palabras clave: Infecciones por VIH; Linfadenitis tuberculosa; Síndrome inflamatorio de reconstitución inmunitaria; Linfadenopatía; Terapia antirretroviral; informe de caso

Introduction

HIV infection remains a significant risk factor for the development and dissemination of tuberculosis (TB), especially in patients with severe immunosuppression. Initiation or re-initiation of antiretroviral therapy (ART) in HIV-infected patients can trigger Immune Reconstitution Inflammatory Syndrome (IRIS), often complicating the clinical course of TB. Tuberculous lymphadenitis is a common extrapulmonary manifestation of TB; however, the presentation of large, necrotic, suppurative lymphadenopathy as part of IRIS is unusual and poses diagnostic and therapeutic challenges[1].

Its pooled estimated incidence among patients with HIV-associated TB initiating antiretroviral therapy was 18% (95% CI 16-21%)[2]. Pulmonary infiltrates and lymph node involvement were the commonest clinical features of paradoxical TB-IRIS reported[2]. Imaging modalities, such as computed tomogra-

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phy (CT), play a crucial role in characterizing the extent and nature of lymph node involvement in suspected cases[3]. This report describes a rare case of IRIS-associated tuberculous lymphadenitis presenting as extensive bilateral cervical lymphadenopathy in a patient with advanced HIV.

Case Report

A 53-year-old woman with a longstanding HIV infection (diagnosed in 2015) experienced severe immunosuppression, with CD4 28 cells/μL and HIV viral load (VL) >1,000,000 copies/mL after discontinuing antiretroviral therapy (ART) for 10 months (early 2020). She restarted ART (day 0, December 2020), achieving viral suppression (VL <20 copies/mL by day 30) and immunological recovery (CD4 89/μL at month 1). On Day 14, she developed pulmonary tuberculosis with ARDS and bronchogenic dissemination, confirmed by sputum GeneXpert MTB/RIF PCR (rifampin-sensitive) and Löwenstein-Jensen culture (sensitive to first-line antituberculous drugs).

In Month 3 (day 90), the patient discontinued both anti-TB and ART. On Day 120, the patient was readmitted without any active complications. Immunovirological assessment showed significant immune recovery with a $CD4^+$ T-cell count of 138 cells/μL (8.2%, +110 cells/μL increase from a baseline of 28 cells/μL) and an HIV viral load of <20 copies/mL, confirming a successful ART response. At this point, she restarted dual therapy (ART + HRZE). Four weeks later (day 150), she developed extensive bilateral cervical lymphadenopathy with fistulous tracts (CD4 156 cells/μL [+128 increase], VL <20 copies/mL), fulfilling the paradoxical TB-IRIS criteria. Cervical computed tomography revealed multiple large necrotic lymph nodes at the bilateral level Vb. The largest lymph node measured approximately 47 × 30 × 49 mm on the right and 45 × 20 × 27 mm on the left (Figure 1). Thoracic CT revealed multiple bilateral nodules and micronodules, with a centrilobular and peribronchial distribution, some of which tend to coalesce, forming small consolidations in the left lower lobe posterior and anterior segments, as well as in the superior segments of the left upper lobes.

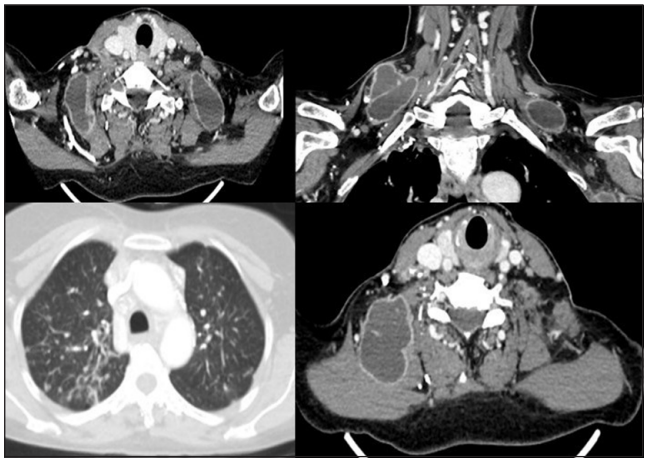

Figure 1. Axial CT scans of the neck and chest at various levels, demonstrating extensive tuberculous cervical soft tissue and abscessed lymphadenopathy, as well as bilateral pulmonary infiltrates.

The diagnosis of paradoxical TB-IRIS was established based on three diagnostic criteria: (1) clinical findings of extensive bilateral necrotic/suppurative cervical lymphadenopathy with fistulous tracts occurring after initial TB control; (2) temporal relationship exactly 4 weeks (Day 150) following dual therapy restart (Day 120); and (3) documented immunological reconstitution with CD4 recovery from 28 to 156/μL (+128 cells/μL increase exceeding the >50/μL threshold) alongside virological suppression (VL <20 copies/mL). Alternative diagnoses were excluded by sterile purulent fluid (MTB PCR/culture negative).

On Day 152, prednisone 1 mg/kg/day was started and tapered for 40 days to manage IRIS inflammation. A percutaneous ultrasound-guided drainage was performed, obtaining 6 mL of purulent fluid, which was sterile for tuberculosis, including PCR analysis. Lately, surgical fistulectomy was performed. By Month 6, partial radiological resolution was achieved, with complete clinical/radiological resolution by Month 12 (CD4 412/μL, VL undetectable).

Discussion

The pathogenesis of IRIS in patients with HIV infection and tuberculous lymphadenitis is complex, because newly initiated ART contributes to an exaggerated inflammatory response, as it does in pulmonary tuberculosis[4]. This case met the established IRIS diagnostic criteria[5]: (1) clinical worsening (extensive necrotic/suppurative lymphadenopathy) after TB diagnosis/treatment; (2) temporal relationship (4 weeks post-ART restart); (3) immunological recovery (CD4 rise from 28 to 156/μL, VL suppression to <20 copies/mL); and (4) exclusion of new infections/drug resistance (sterile pus, drug-sensitive MTB). Paradoxical TB-IRIS occurs in 18% of HIV-TB patients starting ART[2], with lymphadenopathy in 20-30% of cases[1]; however, extensive suppurative cervical involvement with fistulae remains rare (incidence <3%)[6]. Alternative diagnoses, including drug-resistant tuberculosis, treatment failure, lymphoma, and bacterial superinfection, were actively excluded.

Bana et al[1]. reported that 40% of TB-IRIS cases exhibit prolonged lymphadenopathy (>90 days), with lymph node involvement identified as an independent risk factor for chronic inflammation due to persistent mycobacterial antigen reservoirs. Ratcliffe et al[7]. reported a similar cervical TB-IRIS case involving necrotic lymph nodes (maximum diameter of 35 mm) that required drainage. The condition resolved with prednisone at a dosage of 1 mg/kg without ART interruption, reflecting our approach to management. Our case stands out due to the exceptional node size (47×30×49 mm) and bilateral fistulae, exceeding reported dimensions and highlighting the diagnostic role of imaging[1].

Prednisone (1 mg/kg/day) effectively reduced inflammation without requiring ART modification, consistent with Meintjes[8] trial, demonstrating 30% faster resolution compared to placebo (hazard ratio 1.37, 95% CI 1.02-1.84, p=0.03).

The prevention of paradoxical TB-IRIS is an important clinical consideration for high-risk patients. The PredART trial[9] demonstrated that prednisone prophylaxis (40 mg daily for 2 weeks, followed by 20 mg daily for 2 weeks) significantly reduced the incidence of paradoxical TB-IRIS in people living with HIV and TB with $CD4^+$ T-cell counts <100 cells/mm^3 (HR 0.48, 95% CI 0.29-0.79; p=0.004).

No TB regimen intensification was needed (confirmed susceptibility), which avoided toxicity. Full resolution at 12 months (CD4 412/µL) underscores the importance of adherence —repeated discontinuations precipitated this severe IRIS.

The presented case exemplifies the diagnostic complexity of IRIS in HIV-TB coinfection, especially when lymphadenitis manifests with large necrotic nodes and fistulous tracts. Early IRIS recognition prevents unnecessary therapy changes, optimizing outcomes in resource-limited settings where HIV-TB coinfection burdens healthcare systems.

In conclusion, this case illustrates an exceptional presentation of paradoxical TB-IRIS manifesting as disseminated tuberculous lymphadenitis in HIV, featuring unusually large necrotic lymphadenopathies clearly demonstrated by cervical CT, which is crucial for timely diagnosis and multidisciplinary management.

Ethical responsibilities

Protection of persons and animals. This case report followed routine clinical practice and complies with the Declaration of Helsinki. No experimental procedures were performed.

Protection of vulnerable populations. People living with HIV are considered a vulnerable population. Written informed consent for publication (including clinical data and images) was obtained from the patient.

Confidentiality. Clinical data were handled according to institutional protocols. All potentially identifying information has been removed or anonymized, and the signed informed consent is held by the authors.

Privacy. No names, initials, record numbers, or identifiable facial images are disclosed in the manuscript or figures.

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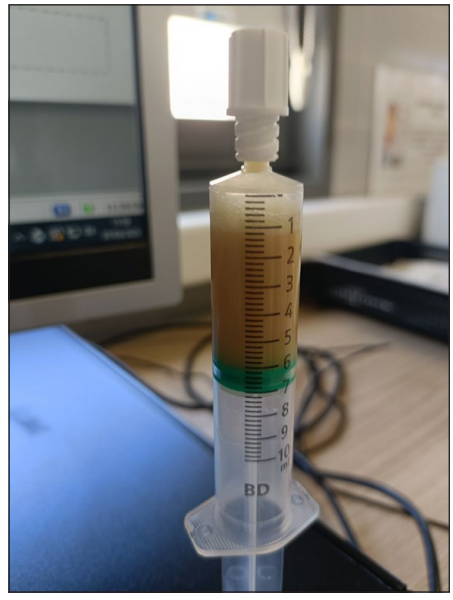

Figure 2. Purulent material (6 mL) obtained by ultrasound-guided percutaneous drainage from cervical lymphadenopathy during TB-IRIS episode.

Authors´ contribution. Conceptualization: FJD, EDS. Data curation: FJD, ARP. Formal analysis: EDS. Investigation: FJD, ARP. Methodology: FJD. Project administration: EDS. Resources: ARP. Supervision: ARP. Validation: FJD, EDS. Visualization: EDS. Writing—original draft: FJD. Writing—review & editing: FJD, EDS, ARP. All authors contributed to read and approved the version of the submitted manuscript.

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