Lepromatous Leprosy in an Immunosuppressed Patient Due to Renal Transplantation Associated with Glucose-6-Phosphate Dehydrogenase Deficiency: A Diagnostic and Therapeutic Challenge

Dear Editor,

Leprosy, declared "eliminated" by WHO in 2000, persists globally with 165,459 cases recorded in 2022.[1] Leprosy in solid organ transplant recipients remains rare, with a few documented examples.[2,3] This case report explores the complex challenges in diagnosing and treating leprosy in solid organ transplantation, characterized by intricate polypharmacological treatments and immunomodulatory drugs.

A 56-year-old male, originally from Senegal but residing in Spain since 1996, presented to the dermatology department in november 2022 with multiple elastic nodules on his upper extremities and face [Figure 1]. These lesions persisted for two months without accompanying symptoms or loss of thermosensory sensitivity. The patient had a kidney transplant in 2014 due to interstitial nephropathy, necessitating ongoing immunosuppression with tacrolimus and sirolimus.

Despite no reported contact with leprosy patients, the patient's regular travel to Senegal and annual two-months stay during summer raised exposure concerns. Histopathological examination of cutaneous lesions revealed a distinct interstitial inflammatory infiltrate primarily composed of histiocytes and numerous polymorphs, along with eosinophilic granular accumulations ("globi") [Figure 2] confirmed via Fite-Faraco staining [Figure 3]. The polymerase chain reaction (PCR) was performed confirming the diagnosis of lepromatous leprosy.

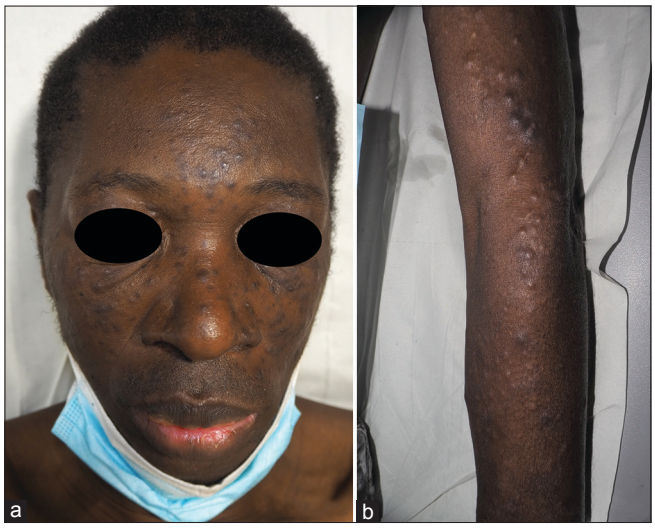

Figure 1: (a) Facial involvement with multiple elastic papulonodules. (b) Similar characteristic lesions distributed on the extremities

Before starting standard therapy (rifampicin, dapsone, clofazimine), the nephrology department optimized immunosuppression, discontinuing sirolimus and maintaining dual tacrolimus-prednisone therapy. A rifampicin-tacrolimus interaction risk was identified, leading to substituting rifampicin with 100 mg/day minocycline. Glucose-6-phosphate dehydrogenase (G6PD) deficiency testing was positive, guiding the replacement of dapsone with 400 mg/day norfloxacin. The initiated treatment included minocycline, clofazimine (100 mg/every other day), and norfloxacin for 18 months.

Upon diagnosis, a suspected leprosy type-2 reaction emerged, causing edema and pain in the right hand and nodules on the arm. This necessitated 30 mg/day of prednisone. After four months on the prescribed regimen, prednisone was gradually tapered. Treatment was well-tolerated, with no reported adverse effects. Some skin lesions improved, but a few nodules persisted, and a decrease in the bacillary index to 2+ at the 4 months' evaluation. Renal function remained stable since antibiotic therapy initiation.

The impact of immunosuppressive therapy on leprosy's incidence, progression, and clinical presentation remains uncertain. Immunosuppression appears to have little effect on HIV-positive patients with low T lymphocyte levels, but cases of immune reconstitution inflammatory syndrome

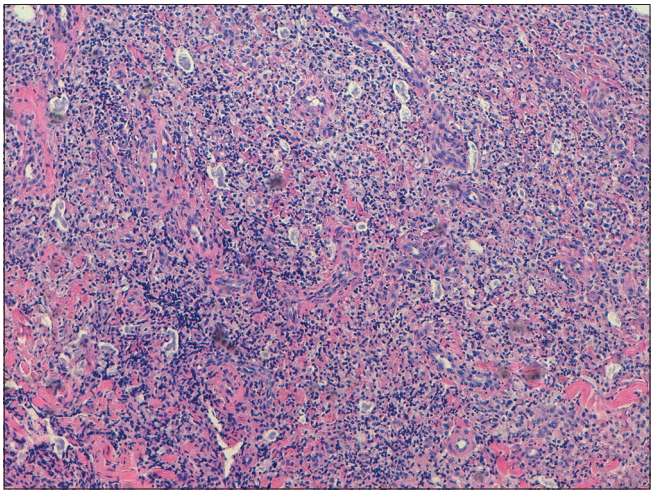

Figure 2: An extensive interstitial inflammatory infiltrate occupying the entire dermal thickness, predominantly composed of histiocytes with abundant clear cytoplasm and granular appearance, as well as polymorphonuclear leukocytes with leukocytoclasis. Notably, numerous accumulations of homogeneous eosinophilic granular material ("globi") are observed among the inflammatory cellularity. This infiltrate is distributed between collagen fibers, which exhibit marked hyalinosis, and enclose annexal, vascular, and erector pili muscle structures (H and E , 20X)

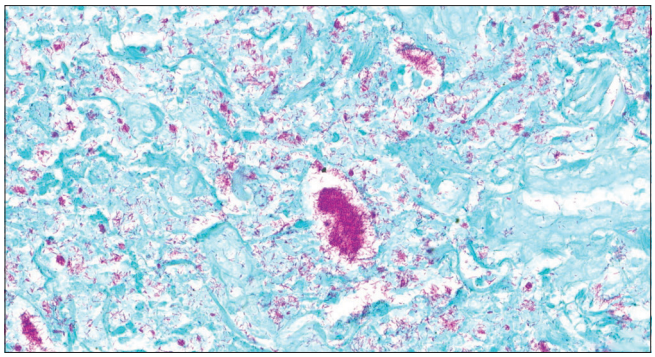

Figure 3: Fite-Faraco staining, shows highly stained clusters of bacilli ("globi")

linked to leprosy and leprosy reactions mediated by T helper cells, regulatory T lymphocytes, and inflammatory cytokines have been reported.[3,4]

Reported cases of leprosy in solid organ transplant patients, including the largest series dating back to 2011,[2] underscore the dearth of information and guidelines for managing these individuals. Challenges arise from limited treatment insights, uncertain immunosuppression-leprosy associations, and the lack of tailored clinical management guidelines.

To the best of our knowledge, this is the first documented instance of a solid organ transplant recipient with G6PD deficiency undergoing immunosuppressive drug treatment affected by leprosy.

Our case, nodules appearing 8 years post-kidney transplant, raises questions about infection source and timeline. The challenge lies in determining whether it's latent leprosy reactivation from his time in Senegal or an acquisition during visits. Given Spain's low leprosy incidence, importation seemed likely.

Regarding the type-2 reaction, it occurred concurrently with the initiation of leprosy treatment and the discontinuation of sirolimus, which may suggest a potential component of autoimmune reconstitution syndrome without alteration of renal function or the onset of symptoms suggestive of organ rejection.

The challenge in this patient lay in the pharmacological treatment. According to the 2018 WHO guidelines for multibacillary leprosy treatment, first-line therapy is multidrug therapy (MDT) involving rifampicin, dapsone, and clofazimine for 12 months.[5] Trindade *et al*.'s[2] case review, including immunosuppressed solid organ transplant patients, administered MDT to 9 of 15 cases with varying durations. Of these, eight cases improved or fully recovered, while one case resulted in death after 5 months. The remaining six patients received diverse antibiotic combinations, including thioamides, fluoroquinolones, and tetracyclines.

Our approach involves minocycline and norfloxacin, in accordance with WHO recommendations that advocate for quinolones such as ofloxacin, moxifloxacin, and levofloxacin for rifampicin-resistant cases. Extending treatment by 6 months' parallels WHO guidelines for non-immunocompromised patients. Addressing the leprosy type-2 reaction, a descending corticosteroid regimen mitigated symptoms.

Furthermore, like prior cases in immunosuppressed solid organ transplant patients, this one represents multibacillary leprosy. Trindade *et al*.[2] also noted this pattern. In contrast, immunocompetent individuals typically exhibit tuberculoid leprosy, suggesting intricate immune interactions leading to increased bacterial load and diminished cellular responses.

In conclusion, the intricate interplay between immunosuppression and leprosy necessitates tailored approaches. Managing leprosy in immunosuppressed transplant recipients requires customized strategies. Collaborative research is crucial for comprehensive guidelines.

Ethical approval

CEIM Hospital General de Granollers 2022/037.

Declaration of patient consent

Consent for the publication of recognizable patient photographs or other identifiable material was obtained by the authors and included at the time of article submission to the journal stating that all patients gave consent with the understanding that this information may be publicly available.

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Conflicts of interest

There are no conflicts of interest.

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