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Tuberculosis and Leprosy Coinfection: A Perspective on Diagnosis and Treatment

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Both leprosy and tuberculosis (TB) are known to have similar geographic endemicity. In the setting of coinfection, interferon-gamma release assays (IGRAs) to detect latent TB can be falsely positive. We report a case of leprosy with a positive IGRA and asymptomatic active pulmonary TB. Minocycline and dapsone therapy was initiated during the workup for TB and changed to rifampin (Rif), isoniazid, pyrazinamide, and ethambutol, with the addition of dapsone once coinfection was confirmed. Our review of the literature revealed a preponderance of coinfection reported with borderline and lepromatous disease. Ten patients were diagnosed with leprosy as the first infection; 7 of these patients (70%) were treated with Rif before TB diagnosis, and 70% (7/10) of coinfected patients were on steroids. If treatment for leprosy is a consideration before ruling out active TB, then minocycline may temporarily replace the Rif. The dire implications of Rif monotherapy in undiagnosed coinfection may warrant chest radiography with or without sputum microbiology as routine initial workup for all leprosy cases.

Keywords. coinfection; leprosy; resistance; steroids; tuberculosis.

Both leprosy and tuberculosis (TB) are known to have similar geographic endemicity [1, 2], and TB needs to be ruled out in cases of leprosy before treatment is initiated with rifampin (Rif)-based regimens. The use of protein-based interferon-gamma release assays (IGRAs) to test for latent TB is confounded by the cross-reactivity of T-cell response with the protein homologs in *Mycobacterium leprae* [3, 4]. The Purified Protein Derivative (PPD) skin test may have some utility in the diagnosis of latent TB in the setting of paucibacillary leprosy (PBL); however, "giant reactions" to PPD testing have been documented in mono-infection with multibacillary leprosy (MBL) [5, 6].

CASE REPORT

A 32-year-old Marshallese woman presented with osteomyelitis of the left third distal phalanx, multiple burn wounds on both hands (Figure 1), and hypopigmented skin lesions (Figure 2) with reduced thermal sensation for several months. A limited disarticulation of the distal phalanx and slit skin smears of hypopigmented skin were performed at the National Hansen's Institute. The smears were Fite stain negative for acid fast bacilli (AFB); however, polymerase chain reaction (PCR) was positive for *M. leprae*. Initial TB workup showed a positive IGRA and PPD skin test greater than 15 mm, and chest radiography (CXR) showed a subtle infiltrate in the right middle lobe, raising suspicion for active TB despite lack of respiratory symptoms. The patient's sputum was AFB smear negative but culture positive for drug-susceptible TB. During the above workup for TB, minocycline and dapsone therapy was initiated for 2 months and was changed to Rif, isoniazid (INH), pyrazinamide, ethambutol (RIPE therapy) with the addition of dapsone once sputum cultures were reported. Repeat sputum cultures after 1 month of RIPE therapy were negative for TB, and RIPE therapy was consolidated to INH and Rif after 2 months. INH, Rif, and dapsone were continued for 4 months, after which the patient was considered effectively treated for TB. The patient was then placed back on minocycline and dapsone for an additional 4 months, completing a 1-year treatment course for leprosy. One month into therapy, CXR was normal, and at the completion of therapy, she had improvement in skin lesions and overall sense of well-being. The patient did not experience any immunological reactions during the above therapy.

DISCUSSION

In the past 15 years, 13 cases of TB and leprosy coinfection have been published; they are summarized in the Table 1. A preponderance of coinfection was seen with borderline and lepromatous disease cases. The immunological milieu of the host appears to paradoxically influence susceptibility to mycobacterial

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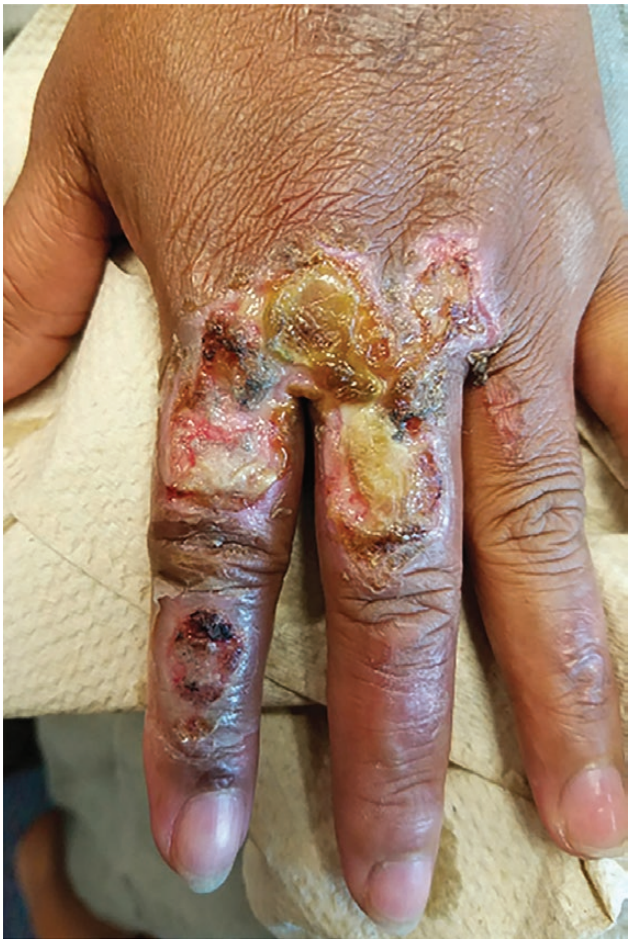

Figure 1. Left hand: burn injury, skin lesions, Fite stain negative, polymerase chain reaction positive for *Mycobacterium leprae*.

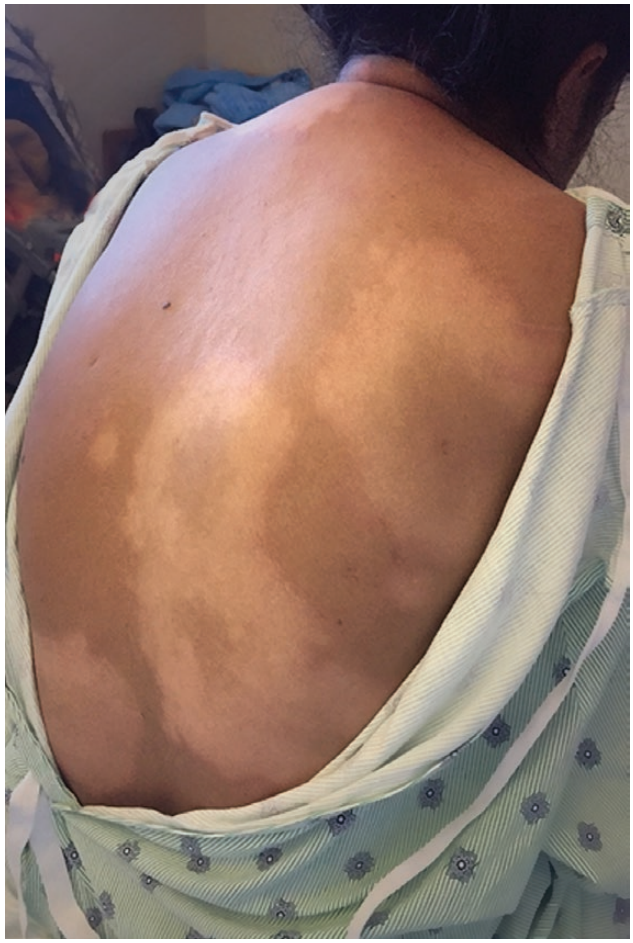

Figure 2. Hypo-aesthetic, hypopigmented lesions on the patient's back.

coinfection, with no consensus regarding whether prior exposure to one offers protection or predisposition to the other. On one end of the spectrum, impaired cell-mediated immunity [7, 8] in patients with MBL may predispose to TB coinfection, whereas among immunocompetent contacts of patients with Hansen's disease in Brazil, the presence of a Bacillus Calmette-Guerin vaccination scar offered 98% protection against MBL [9].

From a treatment perspective, the US Department of Health and Human Services recommends daily Rif [10] in combination with other drugs for the treatment of leprosy across the spectrum. An undiagnosed coinfected patient runs the risk of receiving Rif monotherapy and developing resistance during therapy [11]. In our review, 10 patients were diagnosed with leprosy as the first infection, and of these 10, 7 patients (70%) were treated with Rif before diagnosing TB. Seven of the 10 patients (70%) mentioned above were on steroids before the diagnosis of TB, suggesting that steroids may be a risk factor for reactivation of TB. However, in the TRIPOD studies, no incidence of TB was seen among 300 patients over 24 months who were on prednisone and multidrug therapy for Hansens [12].

CONCLUSION

The clinical implications of failure to identify coinfection cannot be understated, and a positive IGRA or PPD test in a patient with Leprosy should not be considered false positive without ruling out active TB. Rif is a vital component in the treatment regimen for both TB and leprosy, and if treatment for leprosy is a consideration before ruling out active TB, then minocycline may temporarily replace Rif. The dire implications of Rif monotherapy in undiagnosed TB and leprosy coinfection may warrant a CXR with or without sputum microbiology as routine initial workup for all leprosy cases. Additionally, steroid use may be a risk factor for coinfection.

Table 1. Summary of reported cases for coinfection of Leprosy and Tuberculosis within last 15 years

Year/Author	AgeSex	Type of Leprosy	First Infection/TX Given for Leprosy	Gap of Dx	Past Hx of TB	Type of TB	X-Ray/PPD/Interferon	Sputum	Dx of Leprosy	Risk Factors	Lepra Rxn
2003/Lee et al. [13]	62-M	BL	TB	6 mo	NA	Pulm	CXR abnormal	AFB+	Histochem-Fite-Farco, slit skin smear	NA	Type I
2007/Seeramareddy et al. Case #1 [14]	65-M	LL	Leprosy/Dapsone Clofazimine Rifampin	3 mo	No	Pulm	Pleural effusions, CXR w/ infiltrate	AFB+	NA	Steroid	No
2007/Seeramareddy et al. Case #2 [14]	50-M	LL	Leprosy/Thailomide Clofazimine Prednisone	22 mo	NA	Pulm & Perit	CXR cavitary lesions	AFB+	NA	Steroid	Type II
2010/Prasad et al. [15]	34-M	BL	Leprosy/ Dapsone Clofazimine Rifampin	11 mo	No	Pulm	CXR, cavitary lesions, PPD 22 mm	AFB+	Slit skin smear	Steroid	Type II
2013/Trindale et al. Case #1 [16]	31-M	BB-BT	TB	6 mo	NA	Pleural	PPD 14 mm, pleural effusion, CXR abnormal	NA	Hisotchem-Fite-Farco stain	NA	Type I
2013/Trindale et al. Case #2 [16]	46-F	BB-BT	Leprosy/Thailomide Clofazimine Prednisone	1 mo	NA	Pulm	PPD 10 mm, CT chest opacities	AFB+	Hisotchem with anti-BCG	Steroid	Type I
2014/Choubey et al. [17]	34-M	LL	TB	½ mo	No	Pulm	CXR w/ patchy infiltrates	AFB+	Slit skin smear	NA	NA
2014/Rawson et al. [18] Case #1	18-M	LL	Leprosy/Dapsone Clofazimine Rifampin	9 mo	No	Pulm	NA	AFB+	Slit skin smear	Steroid	Silent Neuritis
2014/Rawson et al. [18] Case #2	38-M	LL	Leprosy/Dapsone Clofazimine Rifampin	3 y	No	Extra-Pulm (CNS)	NA	PCR	Slit skin smear	Steroid	Type II
2014/Rawson et al. [18] Case #3	46-M	LL	Leprosy/Dapsone Clofazimine Rifampin	11 mo	No	Pulm	NA	AFB+	Slit skin smear	No	No
2015/Sendrasoa et al. [19]	49-M	LL	Leprosy/Dapsone Clofazimine Rifampin	17 mo	No	Pulm	CT chest opacities	AFB+	Histochem- slit skin smear, PCR biopsy	Steroid	Type II
2015/Verma et al. [20]	38-M	BL	Leprosy/Dapsone Clofazimine Rifampin	7 mo	No	Pulm	CXR cavitary lesions	AFB+	Skin smear	NA	Type II
2017/present author	33-F	TL	Leprosy/Mino Dapsone	2 mo	No	Pulm	CXR opacities, Interferon Gold positive	AFB+	PCR biopsy	NA	No

Abbreviations: AFB, Acid Fast Bacilli; BB-BT, mid-borderline/borderline tuberculoid leprosy; BL, lepromatous borderline leprosy; CXR, chest radiography; LL, lepromatous leprosy; Mino, minocycline; NA, data not available; Neuro, neuritis; PCR, polymerase chain reaction; Perit, peritoneal; PPD, purified protein derivative; Pulm, pulmonary; TB, tuberculosis; TL, tuberculoid leprosy.

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