International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Concurrent Leprosy and Tuberculosis: A Case Study Emphasizing the Importance of Early Detection and Interdisciplinary Management

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Abstract: ***Background: Co-infection of leprosy and tuberculosis(TB) is not uncommon, especially in endemic regions[1]. Host weak immue mechanism state is an important risk factor for such co-infection which is associated with high mortality and major morbidity. Unnoticed leprosy-TB co-infection may predispose to drug resistance, hence clinicians treating tuberculosis must have high index of suspicion of associated leprosy and vice versa. Case presentation: A 52 year old male, with poorly controlled diabetes mellitus who was recently disgnosed to have pulmonary TB, was on ATT had presented with 2 weeks history of paresethesia of legs and bilateral foot drop and thickened peripheral nerves without any skin manifestations, nerve biopsy proven neuritic form of leprosy. Was started on modified MDT for leprosy (includes dapsone and clofazamine, rifampicin was already going as part of ATT). Conclusions: This case highlights the need for a high index of suspicion for co-infection of leprosy and tuberculosis, both of which needs to be treated to avoid drug resistance. Interdisciplinary management and social support are important in these patients.***

Keywords: Co-infection, Leprosy, Pulmonary tuberculosis, foot drop, rifampicin

1. Introduction

Leprosy and Tuberculosis (TB) are endemic diseases to India. Current prevalence of leprosy and Tuberculosis in India are 0.4/10, 000 population and 5/10, 000 population respectively[2]. Both of these diseases are of public health importance as they cause significant morbidity and mortality. Not only belonging to same family, these infections share similar transmission route and are more prevalent in low socio-economic populations which are characterized by overcrowding, poor sanitation and malnutrition. Both diseases show a wide spectrum ranging from pauci-bacillary to multi-bacillary disease depending on the host's cell mediated immune response. Among Asian-African countries, significant proportion of the population are latently infected by *M. tuberculosis* and *M. leprae*, however only around 5 % of these infected individuals develop overt clinical TB or leprosy, owing to their weak immune defence mechanisms.

TB may occur in patients with leprosy and vice versa, with predisposing conditions such as malnutrition, diabetes or other immunocompromised states[3]. We report one such case of pulmonary tuberculosis and leprosy in a uncontrolled diabetic male patient.

2. Case Report

52 year male with recently diagnosed diabetes mellitus presented with 8 weeks history of intermittent fever and cough with expectoration and significant weight loss. He was evaluated outside for TB, was found to have sputum positive for acid fast mycobacterium TB bacilli, CXR was suggestive of cavitatory lesion in left upper lobe favoring active Pulmonary TB (figure 1). He was started on ATT – initiation phase with 4 drug weight based regimen (isoniazid, rifampicin, pyrazinamide, ethambutol). He presented to neurology clinic with complaints of both lower limb paresthesias and weakness of 2 weeks duration, On detailed evaluation we found there was bilateral foot drop (figure 2) and sensory disturbances over common peroneal nerve distribution in both legs along with thickened peripheral nerves (including common peroneal nerves, ulnar nerves, retro auricular nerves – figure 3), however there was no evidence of skin lesions/ madarosis. Nerve conduction studies showed conduction block across both fibular neck in peroneal nerves. We suspected pure Neuritic leprosy as a co-infection and proceeded with sural nerve biopsy which was showing diffuse infiltration with mycobacterium lepra bacilli in nerve fascicles (figure 2)- findings favoring pure neuritic form of leprosy. We continued treatment for TB with 4 drug ATT, added Dapsone and Clofazamine for leprosy, as already Rifampicin was going for TB. For paresthesias, Amitryptylline and multivitamins were given. Patient was symptomatically better after 2 weeks and was monitored closely for development of lepra reaction, which was not encountered.

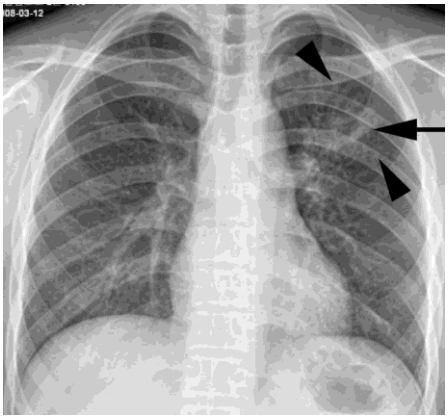

Figure 1: Cavitatory lesion – left upperlobe

Figure 2: Bilateral foot drop

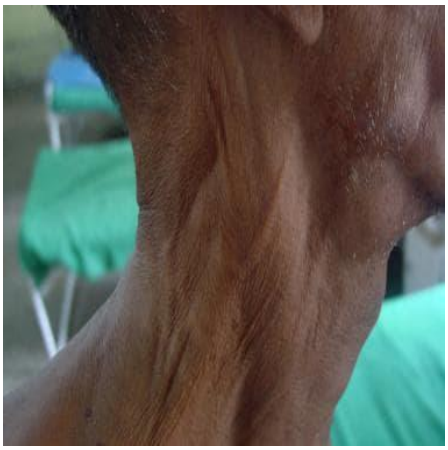

Figure 3: Thickened Nerves

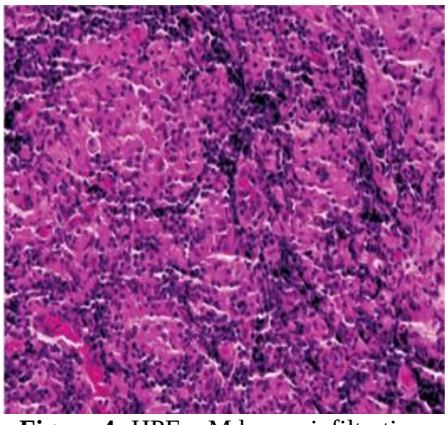

Figure 4: HPE – M.leprae infiltration

3. Discussion

Leprosy (Hansen's disease) is endemic in few parts of the world. As per data, only 14 countries are endemic for leprosy which includes Bangladesh, Brazil, Democratic Republic of Congo, Tanzania, Ethiopia, India, Indonesia, Madagascar, Mozambique, Myanmar, Nepal, Nigeria, Philippines, Sri Lanka and Tanzania.

Ridley and Jopling classified lerosy into five categories:

1) Polar tuberculoid leprosy (TT)
2) Borderline tuberculoid (BT)
3) Borderline borderline (BB)
4) Borderline lepromatous (BL);
5) Polar lepromatous leprosy (LL)

As we go down from the tuberculoid end to the lepromatous end of the spectrum, the bacillary load increases and host immune defence system decrases. Whereas WHO classifies leprosy as paucibacillary leprosy (PB) and multibacillary leprosy (MB) depending on number of skin lesions and bacilli seen on skin smear[4]. PB is characterised by five or fewer skin lesions and no organisms on skin smear, whereas the multibacillary form shows six or more lesions and/or visualisation of bacilli on skin smear. Usually leprosy patients seek medical attention mainly for the dermatological manifestations and careful neurological examination is the key to a successful and timely diagnosis, as there are reports of pure neuritic leprosy which tends to be missed unless suspected by treating doctor.

WHO recommends that any one of the following cardinal signs is diagnostic of leprosy[5]:

1) Hypopigmented or reddish patches with definite sensory loss;
2) Thickened peripheral nerves;
3) Positive skin smears or biopsy material for acid-fast bacilli.

Our patient was on ATT for pulmonary tuberculosis and presented with peripheral neuropathy and bilateral foot drop. Routinely patients on ATT (especially on isoniazid) complaints of paresthesias of limbs which we treat with pyrazinamide, unless we do complete neurological examination including testing for peripheral nerves, we could miss the alternate diagnosis like co-infection with Mycobacterium leprae as in our case. Our patient did not had any skin lesions, but had thickened peripheral nerves with bilateral foot drop, on sural nerve biopsy we found Mycobacterium bacilli in acid fast stain suggesting pure neuritic leprosy.

Review of literature shows co-infection of TB and leprosy with variable time gap between two clinical presentations (Table 1)[6, 7]. Both are chronic granulomatous diseases caused by mycobacteria which are AFB, and the mode of transmission for both is mainly by the aerosol route. However, leprosy caused by *M. leprae*, principally affects the skin and peripheral nervous system, whereas TB caused by *M. tuberculosis* can be pulmonary or extrapulmonary, affecting varied organs.

Conflicting theories have been proposed for the rare reports of leprosy and TB coinfection, with some researchers proposing that the two diseases are antagonistic with a relative protection against dual infection by cross-immunity[8]. This argument is supported by evidence that BCG vaccine also gives some protection against leprosy apart from TB[9]. However, the cross-immunity hypothesis has been countered by a coinfection hypothesis, suggesting that dual mycobacterial infection is not infrequent but in fact, persons with leprosy, especially MB leprosy are more susceptible to TB due to a reduced immune system response[10].

A high mortality rate of 32.7% with Co- infection was confirmed in a recent case review on 156 patients[1].This study also observed that most of the cases of TB were associated with LL (52.5%) followed by BL leprosy (20.5%), while the association of TT leprosy with tuberculosis was uncommon[1]. The time interval between the development of leprosy and TB varies between 2 months and 15 years in one case review[6] .Our patient had co infection of pulmonary TB and leprosy (BL) which is the most common presentation, but association of leprosy with extrapulmonary TB in the form of cutaneous, lymph nodal, laryngeal have also been reported.

Pre-existing comorbid conditions like malnutrition, diabetes mellitus, chronic kidney disease, HIV or treatment with corticosteroids are risk factors for such co-infections .Our patient had Diabetes mellitus as risk factor, with poor glycemic control.

Our patient was already on ATT for TB and we added clofazamine, Dapsone for leprosy (rifampicin was already going as a part of ATT). As per guidelines from World health organization (WHO) and India's National Leprosy Elimination Programme (NLEP)[11]. WHO's MDT regimen for PB and MB leprosy are described in Table 2. Rifampicin is a highly effective bactericidal agent against both M. leprae and M. tuberculosis[12].

Table 1: Comparison of published reports of TB and leprosy coinfection

Author and year	No. of cases	Age/Sex of patient	Symptoms	Gap between both infection	First infections	Type of leprosy (Jopling's)	Type of TB	Predisposing factors	Outcome
Gajwani *et al*[5] 1968	3	60 M 30 M 60 M	Fever, cough, haemoptysis Fever, cough Cough, expectoration	TB Leprosy TB	6 months, diagnosed simultaneously 2 years, diagnosed simultaneously 2 years, diagnosed simultaneously	BT TT BT	Pulmonary	Malnutrition	Unknown
Gupta and Prasad[5] 1971	2	50 M 25 F	Asymptomatic Fever, cough, expectoration	Leprosy Leprosy	1 year, diagnosed simultaneously 6 months, diagnosed simultaneously	TT	Pulmonary	Diabetes, CAD Euthyroid, nodular goitre	Lepra reaction, Better Better
Agnihotri *et al*[5] 1973	3	65 M 18 M 30 F	Fever, emaciation Cough, expectoration, haemoptysis Cough	TB TB Leprosy	1 year, diagnosed simultaneously 4 years, relapse simultaneously diagnosed 1 month	TT	Pulmonary	Malnutrition None	Better
Bhargava and	4	39 M	Fever, cough	Leprosy	3 years	LL	Pulmonary	None	Unknown
Mathur[5] 1976		50 M	Cough, weakness		1 year				
		45 M	Cough, expectoration		4 years			Sputum smear	
		35 M	Cough, expectoration		15 years			None	
Premnath and Ramu[5] 1976	40 cases in 2 years	21 to 64 years (median age: 27)	Cough, expecto-ration (87.5%), fever (57.5%), and weight loss (35%)	Leprosy	1 to 25 years (individual data unavailable)	LL (72.5%); BL (27.5%)	Pulmonary	Malnutrition	Died (30%), left against medical advice (20%), improved (50%)
Ganapathi *et al*[5] 1976	1	30 M	Unknown	Leprosy	Unknown	LL	Cutaneous (lupus vulgaris)	None	Unknown
Vachharajani *et al*[5] 1977	4	50 M 26 M 30 M 29 M	Hypopigmented anaesthetic patches Single hypopigmented anaesthetic patch Macular rash Multiple patches	TB	4 months 4 months 2 months 1.5 months	TT LL TT	Pulmonary	None	Better
Nigam *et al*[5] 1979	20	16 to 58 years (mean age: 28.4) (15 M; 5 F)	Cough, expectoration (100%), fever (80%), weight loss (60%), haemoptysis (25%)	Leprosy	10 to 15 years	LL (15); BL (3); TT (2)	Pulmonary, pleural effusion (2)	Malnutrition	Died (4), left against medical advice (5), Better (11)
Kaur *et al*[5] 1979	2	Unknown	Unknown	Leprosy	4 years	LL	Pulmonary	Malnutrition	Unknown

Gatner *et al*[5] 1980	15 active; 8 healed	Unknown	Unknown	Leprosy	Unknown	LL (4); BL (3); BB (1); BT (7)	Pulmonary	Malnutrition	Improved (10)
Kumar *et al*[4 5] 1982	9	Unknown	Unknown	Leprosy	Unknown	LL (4); BL (3); TT (2)	Pulmonary	Unknown	Unknown
Singh *et al*[5] 1987	25	Unknown	Unknown	Leprosy	Unknown	Individual data unavailable	Pulmonary	Unknown	Unknown
Saha and Rao[5] 1989	18	15 to 65 years (15 M; 3 F)	Unknown	Leprosy	Unknown	Individual data unavailable	Pulmonary	Malnutrition	Unknown
Palki *et al*[5] 1990	1	35 F	Swelling	Leprosy	5 years	BL	Multicentric lupus vulgaris	None	Better
Pinto *et al*[5] 1991	1	36 M	Warty lesion	Simultaneous	occurrence	BT	Cutaneous	None	Jaundice
Inamdar and Sampagavi[5] 1994	1	23 M	Patch, ulcer with discharge	Simultaneous	occurrence	TT	Cutaneous, and Pulmonary	None	Type 1 reaction, better
Arora and Johri[5] 1994	1	40 M	Patch, sinus	Simultaneous	Reoccurrence due to HIV	BL	Lymph nodal	HIV	Better
Agarwal *et al*[5] 2000	1	40 M	Fever, cough, anaesthetic patch	Simultaneous	occurrence	LL	Pulmonary	CKD, transplantation, immunosuppression	Reaction, resolved
Srilakshmi *et al*[5] 2003	1	32 M	Fever, cough	Leprosy	10 years	LL	Pulmonary	None	Dead
Lee *et al*[5] 2003	1	62 M	Cough, expectoration	TB	6 months	BL	Pulmonary	None	Type 1 reversal reaction, better
Agarwal and Sharma[5] 2007	1	36 F	Fever, weight loss	Simultaneous	occurrence	BL	Pulmonary	Rheumatoid arthritis, methotrexate, steroids leflunomide	ENL, better
Sreeramareddy *et al*[5] 2007	2	65 M	Cough, expectoration, chest pain	Leprosy	3 months	BL	Pulmonary, Pleural effusion	Steroid therapy	Better
		65 M	Fever, cough		2 years	LL	Pulmonary	Prednisolone, thalidomide	Better
Prasad *et al*[22] 2010	1	34 M	Breathlessness, loss of appetite, cough, expectoration, skin lesions over face and arms	Leprosy	11 months	BL	Pulmonary	Steroid therapy	Better
Rajagopal *et al*[5] 2012	1	55 M	Swelling and purulent discharge from foot	Simultaneous	occurrence	TT	Extrapulmonary	Diabetes mellitus	Cured
Trindade *et al*[25] 2013	2	31 M	Paraesthetic skin lesions	TB	6 months	BB-BT	Pleural	None	Better
		46 F	Red macules on face and feet	Leprosy	1 month	BT-BB	Pulmonary	Steroid therapy	Better

BL, borderline lepromatous; BT, borderline tuberculoid; CAD, coronoary artery disease; CKD, chronic kidney disease; ENL, erythema nodosum leprosum; LL, lepromatous leprosy; TB, tuberculosis; TT, polar tuberculoid

Table 2: Leprosy treatment regimens currently used worldwide

The WHO MDT regimen[9]	PB: rifampicin 600 mg monthly plus dapsone 100 mg daily; six cycles in 9 months MB: rifampicin 600 mg plus clofazimine 300 mg monthly and dapsone 100 mg plus clofazimine 50 mg daily;12 cycles in 18 months
US National Program treatment[28]	PB: dapsone 100 mg daily plus rifampicin 600 mg daily for Hansen's Disease 1 year. Follow-up every 6 months for 5 years MB: dapsone 100 mg daily plus rifampicin 600 mg daily plus clofazimine 50 mg daily for 2 years. Follow-up every 6 months for 10 year
Intensive regimens[28]	PB: dapsone 100 mg daily for 5 years MB: rifampicin 600 mg daily for 3 years plus dapsone (100 mg/day) indefinitely

MB, multibacillary leprosy; MDT, multidrug therapy; PB, paucibacillary leprosy

4. Conclusion

Co-infection of mycobacterial infections - leprosy and tuberculosis (TB) can occur, though infrequently reported. Delay in recognition of such cases of dual infections may result in poor outcomes if not detected and treated at correct time. Hence TB should not be overlooked in patients with leprosy and vice versa as partial treatement will give rise to emergence of resistant cases, which will be difficult to treat.

Conflict of interest: NIL

Informed and written consent from patient was taken.

References

[1] Rajagopala S, Devaraj U, D'Souza G, *et al*. Co-Infection with *M. tuberculosis* and *M. leprae*—case report and systematic review. *J Mycobac Dis* 2012;2:118.
[2] National Leprosy Eradication Programme (NLEP)—progress report for the year 2013- 14 [Internet]. 2017.
[3] Rawson TM, Anjum V, Hodgson J, *et al*. Leprosy and tuberculosis concomitant infection: a poorly understood, age-old relationship. *Lepr Rev* 2014;85:288–95.
[4] World Health Organization. WHO recommended MDT regimens [Internet]. 2017 http://www.who.int/lep/mdt/regimens/en/

[5] World Health Organization (WHO). *WHO: Weekly epidemiological record Relevé épidémiologique hebdomadaire*. . Geneva: World Health Organization, 2016:21. 421–8.
[6] Prasad R, Verma SK, Singh R, *et al*. Concomittant pulmonary tuberculosis and borderline leprosy with type-II lepra reaction in single patient. *Lung India* 2010;27:19.
[7] Trindade MÂ, Miyamoto D, Benard G, *et al*. Leprosy and tuberculosis co-infection: clinical and immunological report of two cases and review of the literature. *Am J Trop Med Hyg* 2013;88:236–40.
[8] Lietman T, Porco T, Blower S. Leprosy and tuberculosis: the epidemiological consequences of cross-immunity. *Am J Public Health* 1997;87:1923–7.
[9] Setia MS, Steinmaus C, Ho CS, *et al*. The role of BCG in prevention of leprosy: a meta- analysis. *Lancet Infect Dis* 2006;6:162–70.
[10] Donoghue HD, Marcsik A, Matheson C, *et al*. Co-infection of *Mycobacterium tuberculosis* and *Mycobacterium leprae* in human archaeological samples: a possible explanation for the historical decline of leprosy. *Proceedings of the Royal Society B: Biological Sciences* 2005;272:389–94.
[11] Malathi M, Thappa DM. Fixed-duration therapy in leprosy: limitations and opportunities. *Indian J Dermatol* 2013;58:93
[12] Kasper D, Fauci A, Hauser S, *et al*. *Harrison's principles of internal medicine*. 19th ed, 2015