Respiratory System Involvement in Leprosy [1]

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All tissues of the body are known to be affected by leprosy except lung parenchyma and the central nervous system ([13]). The involvement of the nose with nasal discharge rich in leprosy bacilli was described as early as 1891 by Goldschmidt ([17]) and later by Koch in 1897 ([25]), Sticker in 1897 ([46]), and Schaffer in 1898 ([45]). The nasopharynx and larynx are frequently involved in lepromatous patients ([12, 23, 36, 41]). Various degrees of tracheo-bronchial involvement have been described ([7, 30, 37]). *M. leprae* were demonstrated in bronchial washings of two lepromatous patients ([3]). Nasal involvement akin to that of humans has been described in immunologically compromised mice experimentally infected with leprosy bacilli.

The present study is an attempt to elucidate the extent of leprous involvement of the respiratory system in patients and its correlation with its functional impairment.

MATERIALS AND METHODS

Twenty-five patients having leprosy were randomly selected from the leprosy clinic of the dermatology department of the Post-Graduate Institute of Medical Education and Research, Chandigarh, India. A detailed history and clinical examination of the patients with particular emphasis on the respiratory system involvement were recorded on a special chart. Routine investigations of blood, urine, stool and serum biochemistry, were performed. Smears were made and cultures done thrice for acid-fast bacilli from the sputum of each patient. Postero-anterior and lateral chest X-rays of all patients were taken to exclude pulmonary tuberculosis. Anterior and posterior rhinoscopy and detailed laryngoscopic examination were carried out to detect the presence of nasal obstruction, septal ulceration and perforation, destruction of the nasal bridge, congestion or pallor, infiltration, nodularity and atrophy of the nasal mucosa and turbinates and their sensitivity to painful stimuli. The epiglottis, ary-epiglottic folds, and the false and true vocal cords were examined for thickening and nodulation, congestion, pallor and loss of sensation. The oral cavity was examined for involvement of tongue, palate, tonsillar pillars and pharyngeal wall.

Four nasal smears were taken from each nostril (anterior and posterior site on the septum and from inferior and middle turbinates). The smears were stained by the technic of Fite *et al* ([16]). The Bacteriologic Index (BI) and the Morphologic Index (MI) were calculated according to Ridley's logarithmic scale ([42]) and by the method of Waters and Rees ([55]), respectively.

Bronchoscopic and laryngoscopic examinations were carried out under general anesthesia, and the presence of infiltration, nodularity, pallor of mucosa or excessive secretions in the tracheo-bronchial tree were sought. In the absence of any suspicious area, the mucosal tissue was biopsied from the right upper and lower bronchi, the free margin of the epiglottis and the false vocal cords. Smears of tracheal and bronchial secretions were studied for the presence of leprosy bacilli and Bacterial Indices were claculated as described earlier. Biopsy specimens were stained with hematoxylin-eosin and Ziehl-Neelsen stains.

Biopsies were studied for leprous granulomas, presence of acid-fast bacilli and non-specific inflammatory reaction. According to the degree of chronic inflammatory response, the histopathologic findings were classified as mild, moderate or severe.

RESULTS

Twelve patients were classified as lepromatous (LL), eight were borderline (BT, BB, BL), and five were of the tuberculoid (TT) variety. There were 22 males (88%) and 3 females (12%). The ages ranged from 16 to 70 years. Duration of the symptoms varied from two months to ten years with an average of

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50.84 ± 31.68 months. Eleven patients had received dapsone in the past and one was on antituberculosis treatment as well. Signs and symptoms pertaining to the respiratory system are listed in Table 1. Fifteen patients had a dry cough (60%) and 11 in this group were smokers; 12 had a cough with expectoration (48%); 15 had been cigarette smokers from 4 to 30 years, the average duration being 13.20 ± 6.8 years.

TABLE 1. *Symptoms and signs pertaining to the respiratory tract in leprosy patients.*

Symptoms and signs	No. of patients	Percentage (%)
Epistaxis	16	64
Cough	15	60
Expectoration	12	48
Nasal obstruction	12	48
Septal perforation & ulceration	8	32
Depressed bridge of nose	6	24
Anosmia	1	4
Pale mucosa of nose	5	20
Congested nasal mucosa	5	20
Atrophy of turbinates	4	16
Pale mucosa of oral cavity	4	16
Hemoptysis	5	20
Vocal cord thickening	4	16
Nodulation and congestion	4	16
Sluggish arytenoid	3	12
Pale mucosa of larynx	2	8
Thickening of epiglottis	2	8
Diminished sensation of larynx	2	8
Pale tracheal mucosa	5	20

Investigations revealed mild anemia in ten patients (hemoglobin below 12 gm%) and moderate in three (hemoglobin below 10 gm%). Total serum proteins were low in one patient (< 5.5 gm%), serum albumin was low (< 3.2 gm%) in thirteen patients, and hyperglobulinemia (> 3.5 gm%) was present in five patients.

Nasal smears were positive for acid-fast bacilli in eight patients, seven of these (58.3%) were lepromatous (LL) and one (12.5%) was borderline (BB). The BI varied from 1+ to 3+ and the MI from 20% to 83%. Sputum smears were positive for acid-fast bacilli in two patients (Table 2). Cultures did not yield growth on Lowenstein-Jensen medium during six weeks of observation.

Radiologic examination showed bilateral nodular infiltrations in upper and mid-zones of the lungs, without cavitation, in one (LL) patient and was interpreted as being tuberculous in nature. This patient also developed *erythema nodosum leprosum* (ENL) during the hospital stay. Sputum and bronchial smears showed the presence of acid-fast bacilli believed to be *M. leprae*. Culture on Lowenstein-Jensen medium was negative. Evidence of infiltration in the right upper zone was present in another patient, this was also considered tuberculous in nature but cor-

TABLE 2. *Acid-fast bacilli positivity in different specimens.*

Site/Specimen	Bacillary positive				Bacillary negative	
	Lepromatous n = 12		Borderline n= 8		Tuberculoid n = 5	
	Total no.	Percentage (%)	Total no.	Percentage (%)	Total no.	Percentage (%)
Nasal smear	7	58.3	1	12.5	0	0
Bronchial smear	3	25	0	0	0	0
Sputum smear	2	16.6	0	0	0	0
Laryngeal biopsy	0	0	0	0	0	0
Right upper bronchial biopsy	1	8.3	0	0	0	0
Right lower bronchial biopsy	1	8.3	0	0	0	0

roborative clinical findings were not present.

Bronchial smears yielded acid-fast bacilli in only three lepromatous patients (Table 2). In the absence of any other evidence of tuberculosis, these were taken to be leprosy bacilli in two patients. The third had nodular infiltration on radiography but had no clinical evidence of tuberculosis, and culture on Lowenstein-Jensen medium was negative.

Laryngoscopic examination showed congestion and thickening of the right vocal cord in one patient and the area was biopsied. The biopsy specimens from the epiglottis as studied for inflammatory reaction were classified as mild in six (24%), moderate in ten (40%), and severe in three (12%) (Fig. 1); six specimens showed no abnormality (Table 3). Two specimens showed foam cell structures without acid-fast bacilli in them. One biopsy from a false vocal cord showed a tuberculoid lesion characterized by collections of histocytes, Langhan's giant cells, lymphocytes and a few plasma cells, but there was no caseation (Fig. 2). Mast cells were seen in two biopsies. Biopsies of false vocal cords in eleven patients (50%) showed mild inflammatory reaction, moderate in three (13.6%), severe in four (18.2%), and another four (18.2%) had normal histology. Tissue was inadequate for interpretation in three patients.

Bronchial mucosal tissue was not adequate for study from two upper and five right lower lobe bronchi. Leprous granulomas were not found in any bronchial biopsy. Four (17.4%) upper lobe bronchial biopsies were interpreted as normal, infiltrate was mild in fourteen (60.9%), and moderate in five (20.7%) (Table 3). Excess of mucus secreting cells was seen in four specimens, one showed metaplastic changes, and thickening of the basement membrane was seen in another. Biopsies from the right lower lobe bronchus showed normal histology in three (15%), fourteen (70%) revealed mild, two (10%) moderate, and severe inflammatory response (Fig. 3) was seen in only one (5%) (Table 3). Acid-fast bacilli were present in a clump in

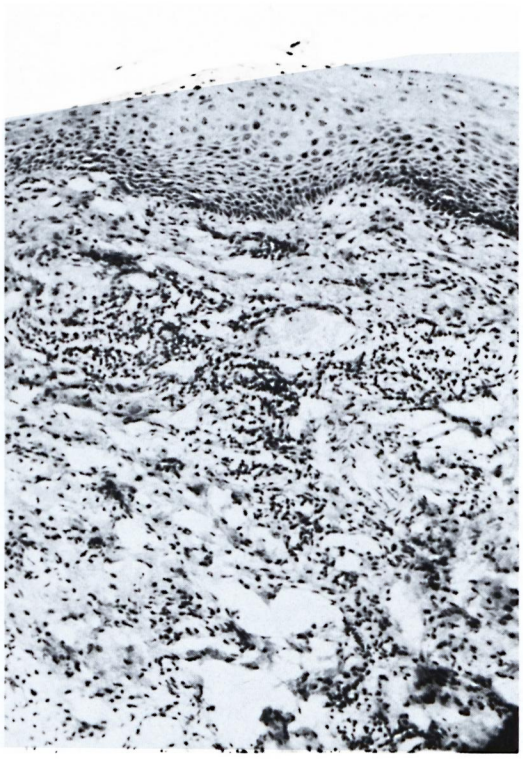

FIG. 1. Section of the epiglottis from LL patient showing diffuse collection of chronic inflammatory cells in the submucosa. H & E, ×100.

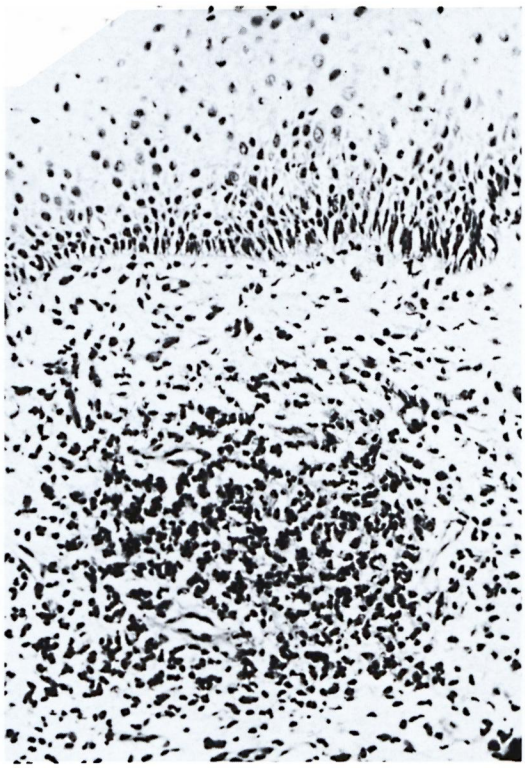

FIG. 2. Section of false vocal cord from the same LL patient showing an inflammatory granuloma under the squamous epithelial layer. H & E, ×100.

the submucosa in one biopsy. Large numbers of mucus secreting cells were present in eight biopsies, metaplastic change in the bronchial epithelium was present in three. Thickening of the basement membrane and eosinophils was seen in one specimen.

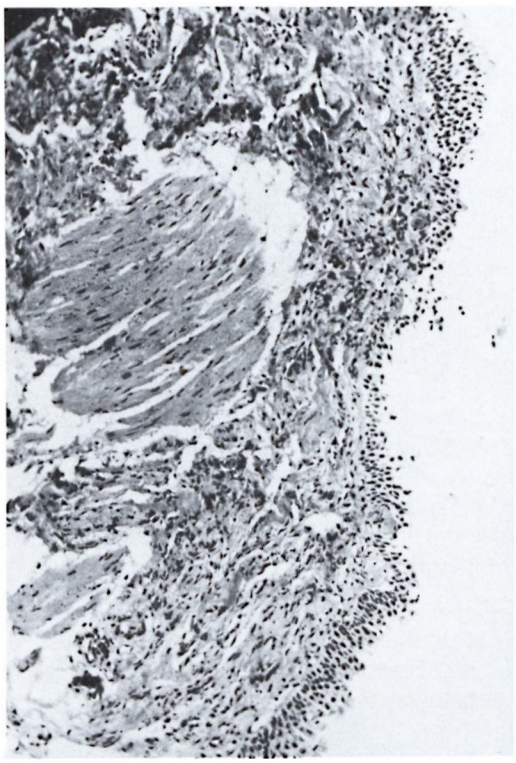

FIG. 3. Section of the right lower bronchus showing partial desquamation of the columnar epithelium. Subepithelial tissue shows inflammation but no foam cells. H & E, ×100.

DISCUSSION

One patient with acid-fast bacilli in sputum, bronchial smears and nodular infiltration of lung fields on radiography had no clinical signs of tuberculosis. Histopathology did not show granuloma or acid-fast bacilli in the bronchial mucosa. Another patient with negative sputum and bronchial smears had acid-fast bacilli in the bronchial biopsy without specific granulomas, clinical or radiologic signs. It is, therefore, evident that there is no correlation between clinical, radiologic, sputum and bronchial smear positivity for acid-fast bacilli and histopathology of bronchial mucosa in the group of patients studied.

Bacillemia in patients with leprosy has been amply documented ([12, 14, 15, 34, 44]). It is, therefore, quite logical to expect various degrees of visceral involvement ([1, 4, 12, 20, 41]).

It was recognized quite early that the nose was frequently involved in leprosy and that nasal discharge contained large numbers of leprosy bacilli ([11, 17, 25, 40, 45]). In the present study the nose was found to be clinically involved in 22 patients (88%). The involvement was in the form of congestion or pallor, septal perforation, ulceration, atrophy of turbinates and depressed nasal bridge. The findings are consistent with those of Barton ([2]) who found nasal involvement in 96% of patients examined. Positive nasal smears for AFB were found in seven (58%) LL patients which conforms to the findings of Davey and Rees ([11]) whose figure was 53%. A positive nasal smear was found in only one patient (12.5%) having borderline leprosy. However, Pedley ([40]), Davey and Rees ([11]), and

TABLE 3. *Incidence of nonspecific inflammatory response in various parts of the tracheo-bronchial tree.*

Site of biopsy[a]	Degree of inflammation vs. no. of patients			
	Normal	Mild	Moderate	Severe
Epiglottis (25)	6 (24%)	6 (24%)	10 (40%)	3 (12%)
False vocal cords (22)	4 (18.2%)	11 (50%)	3 (13.6%)	4 (18.2%)
Right upper bronchus (23)	4 (17.4%)	14 (60.9%)	5 (21.7%)	0 (0%)
Right lower bronchus (20)	3 (15%)	14 (70%)	2 (10%)	1 (5%)

[a]Figures in parentheses give total number actually studied.

McDougall *et al* [35] did not find AFB in any borderline leprosy patients.

As early as 1898, Brutzer [7] described a case of nodular leprosy who had stenosis of the larynx and on autopsy showed considerable thickening of tracheal mucosa with enormous masses of leprosy bacilli present while only a few bacilli could be detected in the bronchial mucus membrane. Involvement of the nose, pharynx and larynx has been described in various studies on LL patients [4, 5, 12, 19, 22, 36, 41]. In the present study, eight patients (32%) had laryngeal involvement. Barton [2] had the same percentage of his patients similarly involved, the most common site of involvement being the epiglottis while in our study the vocal cords were the most frequent site involved. *M. leprae* and granulomas were not found in any of the patients. Powell and Swann [41] found vacuolated histiocytes and globi in many of their 50 autopsy specimens. Desikan and Job [12] found lepromatous granulomas involving the submucosa of the larynx in eight of their nine patients even when none of them showed gross clinical involvement, while Bernard and Vazquez [4] found lepromas in only 2 of their 60 autopsy specimens.

M. leprae were seen by Bedi *et al* [3] in bronchial washings in two patients. In our study, only three patients (25%) of the LL type showed the presence of AFB in bronchial smears. One patient had coexisting pulmonary tuberculosis but none of his specimens grew AFB on Lowenstein-Jensen medium, therefore these were assumed to be leprosy bacilli. Muir [37] stressed the nodular infiltration of the trachea and bronchi which could sometimes rupture to discharge leprosy bacilli, leading to a false diagnosis of pulmonary tuberculosis. Lie [27] described tracheal and bronchial mucosal thickening in two of his three cases, and on microscopy found leprosy bacilli in the epithelium, connective tissue and even in the nerves. Bacilli were found in the mucosa of medium sized and finer bronchioles, but less in number than in the upper portions of the tract. Bernard and Vazquez [4] found *M. leprae* in alveolar macrophages in only 1 of 60 autopsies. However, no bacilli were demonstrated in the tracheo-bronchial tree by other authors [12, 36, 41]. Kirchheimer *et al* [24] in experimentally produced leprosy in the armadillo showed that the lungs had variable histiocytic infiltration with many histiocytes containing globi and individual bacilli. In our study no thickening or nodulation of the bronchial mucosa was seen, leprosy bacilli were seen in two bronchial sections only, and there were no leprous nodules. Culture on Lowenstein-Jensen medium was negative even when one patient had radiologic evidence of tuberculosis. Chronic nonspecific infiltrate in the bronchial wall was seen in the majority (88%) of patients. This could be due to smoking (60%) or other poorly recognized causes. An abundance of mucus secreting cells could also be attributed to similar causes. The association between tobacco smoking and chronic nonspecific lung disease is well recognized.

Negre and Fontan [39] subjected 110 patients to pulmonary radiography and of these 3 patients with ENL showed nodular shadows which were not subsequently visualized the following year. The lesions were considered to be allergic in nature and a manifestation of the general reaction. Two of our patients showed infiltration in the right apical region and the upper and mid-zones. These were considered to be tuberculous. In one patient the lung shadows persisted for six months after the ENL reaction subsided.

Review of the literature reveals a theory of antagonism between leprosy and tuberculosis, i.e., tuberculous infection protects against leprous infection. Chaussinand [9] was the first to put forward this concept on the basis of his observation that as tuberculosis increased in Western countries leprosy decreased. Viel and Dallien [51] also supported this concept, observing only a few cases of tuberculoid leprosy in the local population in the Chuteen mine areas, despite large scale migration of leprosy patients because of rampant tuberculosis in the local population. The relationship also had further documentation [8, 29]. A number of reports have been published from time to time to prove or disprove the relationship between the two diseases [10, 26, 33, 38, 43, 49, 50, 52]. However, some authors [6, 18, 31, 32] have adopted a guarded attitude and regard the evidence as inconclusive.

The incidence of tuberculosis in our study was 8% which is consistent with the studies of other workers [4, 21, 28, 53, 54] who found the incidence to be 11.7%, 8.5%, 11%, and 13.3%, respectively. However, Mitsuda and Ogawa [36], Takano [47, 48], and Desikan and Job [12]

showed involvement with tuberculosis in 70%, 54.7%, and 71%, respectively.

SUMMARY

Respiratory system involvement was studied in 25 leprosy patients, irrespective of age, sex, duration of disease and treatment. Nasal bleeding, cough, expectoration and nasal obstruction were present in 64%, 60%, 48%, and 48% of patients respectively. Sixty percent of the patients were cigarette smokers. Two views of chest skiagrams were taken which showed nodular shadows in upper and midzones in two LL patients. Nasal involvement was present in 88%, chiefly LL and BL patients. Nasal smears taken from four sites were positive for leprosy bacilli in 70.5% of the patients, again LL and BL variety. Anterior and posterior rhino- and laryngoscopic examinations were carried out under general anesthesia and biopsies were taken from the epiglottis, false vocal cords, and the right upper and lower bronchi. Laryngeal involvement was seen in 33% of the patients, chiefly of the LL and BL type. The vocal cords were the most common lesion site. Bronchial smears were positive for leprosy bacilli in three LL (25%) patients. Two epiglottic and one vocal cord biopsy showed foam cell and tuberculoid granuloma. Leprous granuloma was not seen in any bronchial biopsy. Acid-fast bacilli were present in one right upper and lower bronchial biopsy but were absent in laryngeal biopsies. Coexistent pulmonary tuberculosis was present in two LL (8%) patients. No correlation was found between clinical, radiologic, sputum and bronchial smear positivity for acid-fast bacilli and histopathology of bronchial mucosa.

RESUMEN

Se estudió la afección del sistema respiratorio en 25 pacientes con lepra, independientemente de su edad, sexo, duración de la enfermedad y tratamiento. Sangrado nasal, tos, expectoración y obstrucción nasal, afectaron al 64%, 60%, 48% y 48% de los pacientes, respectivamente. El 60% de los pacientes eran fumadores. El exámen radiológico del tórax indicó, en dos pacientes LL, la presencia de sombras nodulares en las zonas superior y media. La afección nasal se encontró en el 88% de los casos, principalmente en los pacientes LL y BL. Los raspados nasales tomados de 4 sitios, mostraron bacilos de la lepra en el 70.5% de los pacientes, otra vez de las variedades LL y BL. Bajo anestesia general, se hicieron exámenes rinolaringoscópicos anteriores y posteriores y se tomaron biopsias de la epiglotis, de las cuerdas vocales falsas y de los bronquios derechos superior e inferior. En el 33% de los pacientes, principalmente de los tipos LL y BL, se encontraron afecciones laríngeas. Las cuerdas vocales fueron el sitio más común de lesión. Las muestras bronquiales de 3 pacientes LL (25%) tuvieron bacilos de la lepra. Dos biopsias epiglóticas y una de cuerdas vocales mostraron células espumosas y granulomas tuberculoides. En ninguna biopsia bronquial se encontraron granulomas tuberculoides. Se encontraron bacilos ácido-resistentes en una biopsia bronquial derecha superior e inferior pero no se encontraron en las biopsias laríngeas. Dos pacientes con LL (8%) tuvieron además tuberculosis pulmonar. No se encontró correlación alguna entre la demostración clínica, radiológica o tintorial en los exudados bronquiales o en el esputo, de bacilos ácido resistentes y la histopatología de la mucosa bronquial.

RÉSUMÉ

Chez 25 malades atteints de lèpre, l'atteinte du système respiratoire a été étudiée, sans qu'il soit tenu compte de l'âge, du sexe, de la durée de la maladie ou du traitement. On a constaté un saignement nasal chez 64% des malades, de la toux chez 60%, des expectorations chez 48%, et une obstruction nasale chez 48% également. La proportion de fumeurs de cigarettes chez les malades atteignait 60%. Deux clichés de skiagramme du thorax furent pris. Ils montraient des ombres nodulaires dans les zones supérieure et médiane chez 2 malades atteints de lèpre LL. Une atteinte nasale était présente chez 88%, principalement chez des sujets atteints de lèpre LL et BL. Des frottis nasaux prélevés à partir de quatre sites étaient positifs pour le bacille de la lèpre chez 70,5% des malades, de noveau appartenant aux types LL et BL. Des examens rhinoscopiques et laryngoscopiques antérieurs et postérieurs ont été pratiqués sous anesthésie générale, et des biopsies ont été prélevées au niveau de l'épiglotte, des fausses cordes vocales, et des bronches droites supérieure et inférieure. Une atteinte laryngée a été constatée chez 33% des malades, principalement des types LL et BL. La lésion la plus commune se situait dans les cordes vocales. Des frottis bronchiques sont révélés positifs pour le bacille de la lèpre chez 3 malades LL (25%). Des cellules spumeuses et des granulomes tuberculoïdes ont été notés au niveau de 2 biopsies de l'épiglotte et d'une biopsie de la corde vocale. Aucun granulome lépreux n'a été observé dans les biopsies bronchiques. Des bacilles acido-résistantes étaient présents dans une biopsie de la bronche droite supérieure et dans une biopsie de la bronche droite inférieure, mais ils étaient par contre absents dans les biopsies laryngées. Une

tuberculose pulmónaire coexistait chez 2 malades LL (8%). Aucune corrélation n'a été observée entre les manifestations cliniques, les images radiologiques, les expectorations, la positivité des frottis bronchiques pour des bacilles acido-résistants, et l'aspect histo-pathologique de la muqueuse bronchique.

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