Original Article

Clinicopathological Correlation of Leprosy and Response to Treatment in Eastern Saudi Arabia

Omar M. Alakloby, Adnan Suliaman Alabdulkareem[1], Salih Hamad M. Aljabre, Mohammad A. Randhawa[2], Esra Omar Alakloby, Abdullah Salih Aljabr[3], Afnan Majed Almutairi

Departments of Dermatology and [3]Family and Community Medicine, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, [1]Department of Dermatology, King Saud Medical City, Riyadh, Saudi Arabia, [2]Department of Pharmacology, Hazrat Bari Sarkar Medical College, Islamabad, Pakistan

Abstract

Background: Leprosy is a chronic, progressing, and disabling disease caused by *Mycobacterium leprae*, predominantly affecting the skin and peripheral nerves. **Aim:** The aim is to study clinicopathological correlation and response to treatment in leprosy patients attending King Fahd Hospital of University (KFHU), Al-Khobar, Eastern Saudi Arabia. **Methodology:** Records of all cases attending Dermatology Department of KFHU from 1985 to 2005 and labeled clinically as leprosy were retrieved. Their clinical data and histopathologic slides were reviewed. Many of the expatriates left Saudi Arabia after diagnosis. The remaining ones and Saudi nationals received the WHO standard treatment for 12 months and 18 months for paucibacillary and multibacillary leprosy, respectively. **Results:** Among 87 cases, there was a good clinicopathological correlation; the most common forms of leprosy clinically and histologically were of borderline leprosy (BB), 31 (35.63%) and 34 (39.08%), followed by tuberculoid type (TT), 22 (25.29%) and 27 (31.03%); lepromatous leprosy, 18 (20.69%) and 17 (19.54%); erythema nodosum leprosum (ENL), 6 (6.9%) and 5 (5.75%); indeterminate leprosy, 4 (4.6%) and 4 (4.6%); and nonspecific, 6 (6.9%). Thirty-two patients received the WHO standard treatment for paucibacillary and multibacillary leprosy, respectively; all cases showed complete clinical improvement with 24-month follow-up, except for two paucibacillary cases who developed ENL and lost follow-up after 16 months. **Conclusions:** There was a good clinicopathological correlation. The response to treatment was good in those who continued treatment and better in TT than lepromatous type of leprosy.

Keywords: Clinicopathological, histopathologic, leprosy, *Mycobacterium leprae*

Introduction

Leprosy is a chronic, systemic, infectious disease of man caused by *Mycobacterium leprae (M. leprae)*.[1] Armauer Hansen, a Norwegian scientist, carried out the first bacterial and epidemiological research about leprosy in 1869.[2] The prevalence of leprosy is variable; the overwhelming majority of cases are found in developing countries.[3]

However, with increasing international immigration and travel, patients with leprosy may present anywhere. According to the Registry of the National Hansen's Disease Programs, 205 new cases were detected in the United States in 2010.[4] Approximately 75% of new cases detected annually in the United States are from immigrants.[5]

In general, leprosy is more common among males with a ratio of approximately 1.5–1.[4] However, some studies report the male-to-female ratio of 2:1.[6] Children are at higher risk of developing the disease when living in endemic areas and exposed to family contacts. The majority of affected children are 10–14 years of age.[6] The respiratory route is probably the most common mode of spread. Nasal discharge from untreated patients with lepromatous leprosy (LL) usually contains large numbers of bacilli.[7]

M. leprae is extremely slow growing, resulting in a long incubation period (2–10 years).[8] Leprosy organisms have never been conclusively grown in artificial medium; however, they have been satisfactorily cultivated in the mouse footpad.[9]

Access this article online

Quick Response Code:

Website: www.jddsjournal.org

DOI: 10.4103/jdds.jdds_53_18

Address for correspondence: Prof. Omar M. Alakloby, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia. E-mail: oamro@iau.edu.sa

How to cite this article: Alakloby OM, Alabdulkareem AS, Aljabre SH, Randhawa MA, Alakloby EO, Aljabr AS, *et al*. Clinicopathological correlation of leprosy and response to treatment in Eastern Saudi Arabia. J Dermatol Dermatol Surg 2019;23:30-4.

Only man and armadillo (*Dasypus novemcinctus*) get leprosy and serve as the reservoir of infection.[10] *M. leprae* is the only bacillary disease with a predilection for nerve tissue.[11] Leprosy is the best example of a disease which has a spectrum from complete lack of host resistance (LL) to effective immunity (tuberculoid leprosy).[12]

In 1966, Ridley and Jopling proposed a classification spectrum of leprosy. This spectrum ranges between two poles: the tuberculoid type (TT) and LL. The center is the borderline leprosy (BB) with two subsidiary forms on each side of BB: borderline tuberculoid (BT) and borderline lepromatous (BL).[13]

The WHO recommendations for the treatment of paucibacillary leprosy (TT and BT) include dapsone 100 mg once daily unsupervised and rifampicin 600 mg once monthly supervised for 6–12 months. For multibacillary leprosy (LL, BL, and BB), recommendations include dapsone 100 mg once daily unsupervised, rifampicin 600 mg once monthly supervised, and clofazimine 50 mg daily unsupervised or clofazimine 300 mg monthly supervised for 2 years.[14]

One Iranian study reported the occurrence of leprosy in relatively older patients (50–55 years),the great majority being male (11:1 ratio), and most of the patients had lepromatous disease; there was poor correlation between clinical and histopathological diagnosis, and the response to treatment was also poor with recurrence in 6/22 (27.3%) due to noncompliance and in another 4/22 (18%) despite complete treatment.[15] However, an Indian study reported male-to-female ratio of 1:1.9, the majority were in the age group of 20–29 years, and there was a good correlation between histopathological and clinical diagnosis, using Ridley–Jopling classification.[16]

Regarding Saudi Arabia, a few studies described the epidemiology of leprosy. Sebai was the first to report about the occurrence of leprosy in Saudi Arabia in 1980 and analyzed the data of 144 patients.[17] Later, Al Sogair *et al*. in 1989 and Ibrahim *et al*. in 1990 described the prevalence of leprosy in the Eastern Province and Southwest of Saudi Arabia, respectively.[18,19] In the late eighties also, Younus and Satti *et al*. reported rare cases of Hansen's disease-causing tonsillitis and lymphadenopathy.[20,21] Soon after that, Arif and Eidarous *et al*. separately reported about divorce among Saudi female leprotic patients.[22,23] Finally, Al Aboud and Al Aboud in 2007 described the occurrence of leprosy in Saudi Arabia, which is mainly based on the data from Ibn Sina Hospital near Jeddah, Southwest of Saudi Arabia, specialized for the patients of leprosy.[24]

The present study was aimed to investigate the clinicopathological correlation, progression of the disease, and response to treatment in patients of leprosy attending a tertiary hospital (King Fahd Hospital of University [KFHU]) in Al-Khobar, Eastern Province of Saudi Arabia.

Methodology

Records of all cases attending Dermatology Department at KFHU, Al-Khobar, Saudi Arabia, during the period from January 1985 to December 2005 and clinically diagnosed as leprosy were reviewed. Their histopathologic slides, stained with hematoxylin and eosin and Wade-Fite stain (W/F), were examined by a dermatopathologist. The percentile presentations of different types of leprosy based on clinical and histopathological diagnosis were determined and correlated with each other. The response to treatment was also evaluated from the clinical improvement. The data of all cases were entered in prescribed forms and their demographic data and clinical and histopathological presentations were analyzed by SPSS version (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago, USA).

Results

Of 25,276 new cases seen in Dermatology Clinic over 20 years (1985–2005), 87 were suffering from leprosy, giving an occurrence rate of 0.34%. Eighteen were Saudi by nationality and 69 non-Saudis. Seventy-seven (88.5%) were male and 10 (11.5%) were female, with a male-to-female ratio of 7.7:1. Their ages ranged between 22 and 40 years, with a mean age of 32 years.

According to the clinical diagnosis, the majority of cases were of borderline leprosy, 31 (36%), followed by tuberculoid, 22 (25%); lepromatous, 18 (21%); erythema nodosum leprosum (ENL), 6 (6.9%); indeterminate, 4 (4.6%); and clinically nonspecific, 6 (6.9%). Likewise, the histopathological diagnosis demonstrated that the majority of cases were of borderline leprosy (BB), 34 (39%), of these 19 were BT and 15 BL leprosy, followed by TT, 27 (31%); LL, 17 (20%); ENL, 5 (5.8%); and indeterminate leprosy (IL), 4 (4.6%). There was a good correlation between clinical and histopathological diagnosis [Figure 1].

Hypopigmented macular lesions were the most common clinical presentation (45 patients, 52%), followed by plaques (22 patients, 25%), nodules (19 patients, 22%),

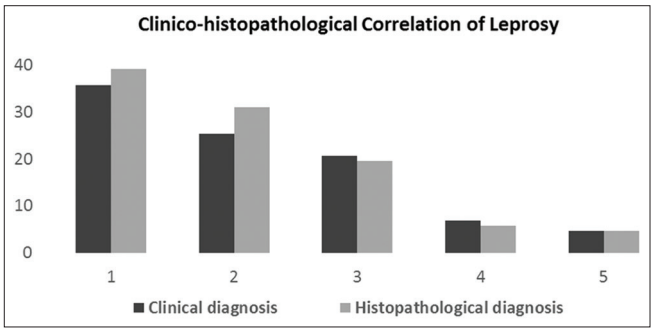

Figure 1: Correlation between clinical diagnosis (dark column) and histopathological diagnosis (light column). Vertical axis shows % prevalence and the horizontal axis gives types of leprosy: (1) Borderline, (2) tuberculoid, (3) lepromatous, (4) erythema nodosum leprosum, and (5) indeterminate leprosy

Table 1: Clinical presentations of lesions in different types of leprosy (*n*=87)

	Hypopigmented macules	Plaques	Nodules	Acquired ichthyosis	Bullae	Painful swellings	Ulcers
TT	16	2	-	-	1	-	1
BT-BL	25	10	4	6	3	2	2
LL	2	9	9	4	-	-	1
ENL	-	1	6	2	-	-	1
INDET-	2	-	-	-	-	1	-
Total	45	22	19	12	3	3	5

Some patients had more than one lesion at a time. TT: Tuberculoid type, BT: Borderline tuberculoid, BL: Borderline lepromatous, LL: Lepromatous leprosy, ENL: Erythema nodosum leprosum, INDET: Indeterminate leprosy

acquired ichthyosis (12 patients, 14%), and ulcers (5 patients, 5.7%) [Table 1].

Thirty-six patients (41%) had skin lesions with decrease in touch sensation and 15 (17%) had skin lesions with loss of sensation. Six patients (6.9%) diagnosed histopathologically as leprosy had skin lesions with normal sensation. Decreased touch sensation was more common in patients with tuberculoid lesions (23/36), followed by LL lesions (11/36); loss of sensation was equal in TT and LL.

The upper colder areas of limbs were the most prevalent sites of involvement (52 patients, 60%). Numerous lesions (>5) was most common, present in 36 patients (41%), while one or few (2–5) lesions were in the remaining patients who had truncal, facial, and lower limb involvement. The ulnar nerve was enlarged in 38 patients (44%), followed by greater auricular nerve and lateral popliteal (7 patients each, 8%), superficial peroneal (6 patients, 6.9%), posterior tibial (3 patients, 3.4%), and supraorbital nerve (2 patients, 2.3%).

Complications of leprosy encountered included neuritis in 8%, orchitis in 5%, epistaxis in 5%, deformity in 5%, secondary infection in 5%, conjunctivitis in 2%, dyspigmentation in 2%, and hemolysis in 2% of patients.

Histopathological sections of all LL types demonstrated *M. leprae*, appearing as globi within macrophages or red bacilli with W/F-stained slides. Organisms were less frequent in BB and neither seen in TT nor in IL type of leprosy. TT lesions exhibited superficial epithelioid granulomas (elongated granuloma) localized around neurovascular bundles with some giant cells within them. Borderline types showed characters of both TT and LL types. LL type also showed infiltration mostly composed of bacillus laden histiocytes (foam cells of Virchow); the infiltrate was localized in the dermis and was separated from the epidermis by a well-defined clear green zone. ENL showed leukocytoclastic vasculitis deep in the dermis (subcutaneous tissues), and bacilli were demonstrated in four of five cases [Table 2].

Many of the expatriates left Saudi Arabia after diagnosis; those who stayed (17) and Saudi nationals (15) continued the WHO standard treatment for 12 months and 18 months for paucibacillary (22) and multibacillary (10) leprosy, respectively. Their response to treatment varied according to the type of leprosy. Patients with paucibacillary showed marked clinical improvement in the first 4–6 months and continued to receive the treatment for 12 months, except two who developed ENL and who were started on prednisolone 1 mg/kg body weight per day and clofazimine 100 mg three times daily in addition to the standard treatment. Unfortunately, due to waxing and waning of symptoms, they lost follow-up after the 16th month. Lesions in patients of multibacillary took longer to clear (10–15 months), and the treatment was still continued for 18 months. The remaining paucibacillary and all multibacillary patients were followed up for 24 months and clinically remained symptom free.

Discussion

The present study was carried out in a teaching and referral hospital, KFHU, Al-Khobar, Saudi Arabia. The number of patients reported reflect the low incidence of leprosy in the Eastern Province of Saudi Arabia (87 patients in 20 years), and most of them were non-Saudis (69 patients, 79.3%). Most of the patients were active adult (20–40 years); as children are the most susceptible group to catch the disease, the long incubation period may contribute to the observed age distribution. Similar age distribution was reported in some studies from India and Saudi Arabia.[24,25] However, an Iranian study reported the ages between 50 and 55 years; the higher ages could be due to delay in diagnosis and referral.[15] In the present study, there was a large difference in sex distribution, with more males than females. This may be explained by the non-Saudi patients who were mostly male workers. An age and sex distribution similar to our study was reported in a neighboring Gulf state, Kuwait; leprosy was mostly in males (75%), average 33.6 years, and non-Kuwaiti immigrants from tropical and subtropical countries (81%).[26]

The histopathological diagnosis correlates well with the clinical diagnosis. Histopathological examination was the main investigative method for all the patients reviewed and the only determinant of the diagnosis in six patients. A similar correlation was reported in other studies.[16,27] The current diagnosis of leprosy, even in the hands of the most experienced dermatologists, is usually years late. One of the effective tools of leprosy control is the screening of high-risk participants like children and household or close contacts of infectious patients. The histopathological examination of

Table 2: Microscopic features of skin biopsy in patients of leprosy ($n=87$)

Type of leprosy	Number	AFB	Epithelial granuloma	Histiocytic granuloma	Mononuclear infiltrate	Neurovascular	Superficial infiltrate	Subcutaneous infiltrate	Green zone	Multinucleated giant cells	Necrosis	Neural involvement	Peri-appendageal involvement
TT	27	0	25	1	3	25	20	4	0	10	3	19	26
BT	19	3	17	4	4	19	6	9	13	6	3	17	19
BL	15	9	11	12	3	14	0	10	14	2	2	15	14
LL	17	17	1	17	2	15	0	15	15	0	1	16	16
ENL	5	4	3	4	0	4	0	5	5	0	0	4	4
IL	4	0	0	0	3	4	3	0	0	0	0	0	0
Total	87												

TT: Tuberculoid type, BT: Borderline tuberculoid, BL: Borderline lepromatous, LL: Lepromatous leprosy, ENL: Erythema nodosum leprosum, IL: Indeterminate leprosy, AFB: Acid fast bacilli

suspected leprosy sections is an effective method of diagnosis and classification.[13]

Multi-drug regimens were used as recommended by WHO, including dapsone and rifampicin for paucibacillary and the addition of clofazimine for multibacillary leprosy. Patients with paucibacillary showed marked clinical improvement in the first 4-6 months, while lesions in patients of multibacillary took longer to clear.

Conclusion

There was a good clinicopathological correlation among all subclasses of leprosy with complete agreement among indeterminate leprosy cases. The response treatment was good especially among paubacillary patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ting P. Leprosy – The living dead: A life of isolation and suffering. In: The Proceedings of 12th Annual History of Medicine Days, Faculty of Medicine, University of Calgary, Health Sciences Center, Calgary AB; 2003. p. 18.
2. Harboe M. Armauer Hansen – The man and his work. Int J Lepr 1973;14:417-24.
3. Global leprosy situation, 2010. Wkly Epidemiol Rec 2010;85:337-48.
4. Available from: http://www.hrsa.gov/hansensdisease/. [Last accessed on 2011 Jun 20].
5. Truman RW, Singh P, Sharma R, Busso P, Rougemont J, Paniz-Mondolfi A, *et al*. Probable zoonotic leprosy in the Southern United States. N Engl J Med 2011;364:1626-33.
6. Patil RR. Determinants of leprosy with special focus on children: A socio-epidemiological perspective. Am J Dermatol Venerol 2013;2:5-9.
7. Abraham S, Mozhi NM, Joseph GA, Kurian N, Rao PS, Job CK. Epidemiological significance of first skin lesion in leprosy. Int J Lepr Other Mycobact Dis 1998;66:131-9.
8. Al-Mubarak R. New Approaches to the Identification of Biomarkers of Infection and Nerve Damage in Leprosy. Thesis Submitted for the Degree of PhD. Colorado State University. Fort Collins, Colorado: Spring; 2012.
9. Shepard CC. The experimental disease that follows the injection of human leprosy bacilli into foot-pads of mice. J Exp Med 1960;112:445-54.
10. Kirchheimer W, Stoors E. Attempts to establish the armadillo as a model for the study of leprosy. I. Report of lepromatoid leprosy in an experimentally infected armadillo. Int J Lepr 1971;39:693-702.
11. Bhat RM, Prakash C. Leprosy: An overview of pathophysiology. Interdiscip Perspect Infect Dis 2012;2012:181089.
12. Scollard DM, Adams LB, Gillis TP, Krahenbuhl JL, Truman RW, Williams DL. The continuing challenges of leprosy. Clin Microbiol Rev 2006;19:338-81.
13. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five-group system. Int J Lepr Other Mycobact Dis 1966;34:255-73.
14. World Health Organization. WHO Model Prescribing Information: Drugs Used in Leprosy. Geneva; 1998.
15. Farshchian M, Kheirandish A. Clinico-pathological study of 12 cases of patients with leprosy admitted in Sina Hospital, Hamdan, Iran, from 1991 to 2000. Int J Dermatol 2004;43:906-10.
16. Moorthy BN, Kumar P, Chatura KR, Chandrasekhar HR, Basavaraja PK.

Histopathological correlation of skin biopsies in leprosy. Indian J Dermatol Venereol Leprol 2001;67:299-301.
17. Sebai ZH. An epidemiological study of leprosy and leprosy care in Saudi Arabia. Saudi Med J 1980;1:133-40.
18. Al Sogair SM, Ellahbadi SL, Namnyak SS. Leprosy in Eastern province of Saudi Arabia. Saudi Med J 1989;10:48-53.
19. Ibrahim MA, Kordy MN, Aiderous AH, Bahnassy A. Leprosy in Saudi Arabia, 1986-89. Lepr Rev 1990;61:379-85.
20. Younus M. Leprosy in ENT. J Laryngol Otol 1986;100:1437-42.
21. Satti MB, al-Mohaya S, Omer AS. Hansen's disease: A cause of lymphadenopathy in endemic areas. Trop Geogr Med 1989;41:80-4.
22. Arif MA. Comment: Divorce among Saudi female leprotic patients: An experience at Ibn Sina Hospital. Lepr Rev 1993;64:166-9.
23. Eidarous AH, Kamel Z, Ahmad F. Divorce among Saudi female leprotic patients: An experience at Ibn Sina Hospital. Lepr Rev 1996;67:343-4.
24. Al Aboud F, Al Aboud K. Leprosy in Saudi Arabia. Lepr Rev 2007;78:405-8.
25. Prasad PV, Babu A, Kaviarasan PK, Viswanathan P, Tippoo R. MDT-MB therapy in paucibacillary leprosy: A clinicopathological assessment. Indian J Dermatol Venereol Leprol 2005;71:242-5.
26. Al-Mutairi N, Al-Doukhi A, Ahmad MS, El-Khelwan M, Al-Haddady A. Changing demography of leprosy: Kuwait needs to be vigilant. Int J Infect Dis 2010;14:876-80.
27. Pandya AN, Tailor HJ. Clinicohistopathological correlation of leprosy. Indian J Dermatol Venereol Leprol 2008;74:174-6.