Clinical Cases in Dermatology
Series Editor: Robert A. Norman

Swetalina Pradhan
Piyush Kumar *Editors*

Clinical Cases in Leprosy

Springer

Clinical Cases in Dermatology

Series Editor
Robert A. Norman, Tampa, FL, USA

This series of concise practical guides is designed to facilitate the clinical decision-making process by reviewing a number of cases and defining the various diagnostic and management decisions open to clinicians.
Each title is illustrated and diverse in scope, enabling the reader to obtain relevant clinical information regarding both standard and unusual cases in a rapid, easy to digest format. Each focuses on one disease or patient group, and includes common cases to allow readers to know they are doing things right if they follow the case guidelines.

Swetalina Pradhan • Piyush Kumar
Editors

Clinical Cases in Leprosy

Springer

Editors
Swetalina Pradhan
Dermatology Venereology and Leprosy
All India Institute of Medical Sciences
Patna, India

Piyush Kumar
Dermatology Venereology and Leprosy
Madhubani Medical College and Hospital
Bihar, India

ISSN 2730-6178 ISSN 2730-6186 (electronic)
Clinical Cases in Dermatology
ISBN 978-3-031-08219-1 ISBN 978-3-031-08220-7 (eBook)
https://doi.org/10.1007/978-3-031-08220-7

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

To our families who generously parted with their time to allow us the privilege of working for this book.

Swetalina Pradhan
Piyush Kumar

Preface

Leprosy, a disease of the skin and peripheral nerves predominantly, is a chronic infectious disease caused by *Mycobacterium leprae*. If the disease is not diagnosed and treated early, peripheral neuropathy, the hallmark of leprosy, may result in various disabilities leading to social stigma and discrimination. Though leprosy has been declared an "eliminated disease" by WHO, globally there were 127,558 new lepro6sy cases detected in 2020 alone. Leprosy is largely restricted to endemic areas, but non-endemic western countries too observe occasional cases of leprosy because of migratory population. Hence, there is a need for renewed interest in research on different diagnostic and management aspects of the disease. However, there have been fewer developments in research and publications partly because of leprosy being declared an eliminated disease. The lack of vaccine combined with lack of newer more effective drugs makes early diagnosis and treatment still the most effective strategy in the management of leprosy cases. Leprosy has been a great mimicker, and often, unusual clinical presentations are encountered in clinical practice. Hence it is very important for clinicians to familiarize themselves with classical as well as unusual forms of leprosy and lepra reaction. The diagnosis of leprosy is most of the times clinical, but various diagnostic tools are increasingly being used to diagnose the disease early in clinically doubtful cases. There have been developments in serological, molecular, electrophysiological and radiological techniques which can help in confirming the diagnosis of leprosy with precision.

This book *Clinical Cases in Leprosy* has been written with an intention to document classical as well as unusual cases of leprosy seen in "post-elimination" era. The book is divided into two parts. The first part is focused on a brief overview of leprosy including clinical classification, clinical examination, investigations, treatment, counselling and rehabilitation. The second part discusses leprosy in a case-based manner and includes the cases that represent the wide variations in clinical features noted in leprosy. Each chapter follows a uniform pattern of description of clinical presentation, followed by differential diagnosis, investigations, final

diagnosis and at last, brief discussion of the case. The chapters are adequately supported with clinical and histopathological photographs for better appreciation of different concepts in leprosy. We are hopeful that the book will help physicians in suspecting and diagnosing leprosy early and in a better efficient management of the cases.

Patna, India
Bihar, India

Swetalina Pradhan
Piyush Kumar

Acknowledgements

We express our gratitude to the authors for working tirelessly on this project and completing the chapters on time.

We are grateful to our teachers for showing us the path.

We thank all our patients, who kept faith in us and taught us a lot.

We thank all our students, past and present: we learn more when we teach.

We are thankful to the Springer staff for doing an excellent job in making this book project a success.

Contents

Contributors

Neeraj Agarwal Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Bibinagar, Telangana, India

Pooja Agarwal Department of Skin and VD, Smt. NHL Municipal Medical College, Ahmedabad, India

Ishan Agrawal Department of Dermatology, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India

P. K. Ashwini Department of Dermatology Venereology and Leprosy, JSS Medical College, Mysuru, Karnataka, India

Sasi Attili Visakha Institute of Skin and Allergy, Vizag, India

Shirin Bakshi Department of Dermatology, Venereology and Leprology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Biswanath Behera Department of Dermatology, Venereology and Leprology, Dermatology, All India Institute of Medical Sciences, Bhubaneswar, India

Abhishek Bhardwaj Department of Dermatology, Venereology and Leprology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

Jatin Chauhan Department of Dermatology, Venereology and Leprosy, Baroda Medical College and SSG Hospital, Vadodara, India

Gaurav Dash Department of Dermatology, Hitech Medical College, Bhubaneswar, India

Anugandha Ghatge Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Medical Sciences, Jawaharlal Nehru Medical College, Wardha, India

Sanjeev Gupta Department of Dermatology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala, India

Saurabh Swaroop Gupta Department of Dermatology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala, India

Sunil Kumar Gupta Department of Dermatology, All India Institute of Medical Sciences, Gorakhpur, India

Kirti Kalra Department of Dermatology, Smt. NHL Municipal Medical College, SCL General Hospital, Ahmedabad, India

Hemanta Kumar Kar Department of Dermatology, Venereology and Leprosy, Kalinga Institute of Medical Sciences, KIIT University, Bhubaneshwar, Odisha, India

Piyush Kumar Dermatology Venereology and Leprosy, Madhubani Medical College and Hospital, Keshopur, Bihar, India

Niharika Ranjan Lal Department of Dermatology, ESI-PGIMSR and ESIC Medical College, Kolkata, India

Bhushan Madke Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Medical Sciences, Jawaharlal Nehru Medical College, Wardha, India

Rajesh Kumar Mandal Department of Dermatology, North Bengal Medical College, Sushrutanagar, West Bengal, India

Paraini Marandi Department of Dermatology, VSS Institute of Medical Sciences and Research, Sambalpur, Odisha, India

Abhisek Mishra Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Bhubaneswar, India

Tarun Narang Department of Dermatology, Venereology and Leprology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Tanmay Padhi Department of Dermatology, Veer Surendra Sai Institute Of Medical Sciences And Research, Burla, India

Maitreyee Panda Department of Dermatology, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India

Abhishek Parekh Department of Dermatology, Venereology and Leprosy, Medical College and SSG Hospital, Vadodara, India

Nibedita Patro Department of Dermatology, Venereology and Leprology, Hi-Tech Medical College and Hospital, Bhubaneswar, India

Malcolm Pinto Department of Dermatology, Venereology and Leprosy, Yenepoya Medical College, Mangalore, India

Somen Kumar Pradhan Department of Community Medicine and Family Medicine, AIIMS, Bhubaneswar, India

Swetalina Pradhan Dermatology Venereology and Leprosy, All India Institute of Medical Sciences, Patna, India

M. Bandhala Ranjan Department of Dermatology, Venereology and Leprology, All India Institute of Medical Sciences, Jodhpur, India

Santoshdev P. Rathod Department of Dermatology, Smt. NHL Municipal Medical College, SCL General Hospital, Ahmedabad, India

Ashmiya Razak Department of Dermatology, Venereology and Leprosy, Yenepoya Medical College, Mangalore, India

Arpita Nibedita Rout Department of Dermatology Venereology and Leprosy, All India Institute of Medical Sciences, Deogarh, India

Kananbala Sahu Department of Dermatology, Sri Jagannath Medical College and Hospital, Puri, India

Pooja Sahu Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Medical Sciences, Jawaharlal Nehru Medical College, Wardha, India

Rashmi Sarkar Department of Skin and VD, Lady Hardinge Medical College, New Delhi, India

Mitanjali Sethy Department of Dermatology, Venereology and Leprosy, Kalinga Institute of Medical Sciences, KIIT University, Bhubaneswar, Odisha, India

Hiral Shah Department of Dermatology, Venereology and Leprosy, Baroda Medical College and SSG Hospital, Vadodara, India

Rashid Shahid Dermatology, Venereology and Leprosy, All India Institute of Medical Sciences, Patna, India

Vikas Shankar Department of Dermatology, Patna Medical College and Hospital, Patna, India

Manjunath Shenoy Department of Dermatology, Venereology and Leprosy, Yenepoya Medical College, Mangalore, India

Shilpa, MSc (Hons) Department of Dermatology, Venereology and Leprology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Ratnakar Shukla Department of Dermatology, All India Institute of Medical Sciences, Patna, India

Suvesh Singh Dermatology, Venereology and Leprosy, All India Institute of Medical Sciences, Patna, India

Chandra Sekhar Sirka Department of Dermatology, All India Institute of Medical Sciences, Bhubaneswar, India

Dependra Kumar Timshina Remedy Clinics, Siliguri, West Bengal, India

Anup Tiwari Yashoda Hospital and Research Center, Ghaziabad, India

Part I
Basics

Chapter 1
Clinical Classification of Leprosy

Tanmay Padhi, Kananbala Sahu, and Swetalina Pradhan

Abstract Leprosy is a chronic disease with varied manifestations. Its varied course, prognosis, and complications require a distinct classification. A uniform classification helps in communication at field level with appropriate diagnosis and management of disease. But at the research level, the perception is different. Here we have described currently available different classifications of leprosy to meet the expectations of both primary healthcare workers and researchers.

Keywords Leprosy · Classification · Ridley-Jopling · WHO classification

Abbreviations

AFB	Acid fast bacilli
MB	Multibacillary
NLEP	National Leprosy Eradication Programme
PB	Paucibacillary
SSS	Slit skin smear
WHO	World Health Organization

T. Padhi (✉)
Department of Dermatology, VIMSAR, Burla, India

K. Sahu
Department of Dermatology, SJMCH, Puri, India

S. Pradhan
Department of Dermatology, AIIMS, Patna, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_1

Introduction

Leprosy can present with cutaneous lesions and/or neural symptoms. The wide variations in disease presentation and its course, prognosis, and complications force one to consider these variants as a distinct entity and need to classify the disease. But a single classification can't meet all the criteria at all levels. Hence, a uniform classification by WHO helps in easy communication among field workers and early diagnosis and treatment of leprosy. The comparison of clinical, histological, bacteriological, and immunological parameters by Ridley-Jopling helps the researchers to understand the finer aspects of the disease.

Classification of Leprosy

Classification of leprosy is important because it decides the line of treatment and stage and prognosis of the disease.

Criteria Deciding Classifications

1. Bacteriological criteria: measures the density of organism in lesions and estimated by slit skin smear technique or in biopsy specimens.
2. Immunological criteria: deficiency of cell-mediated immunity against *M. leprae* is measured by lepromin testing. Patients are classified as lepromin positive (good immunity) and lepromin negative (poor immunity).
3. Histological criteria: it reflects the actual process going on inside the body in the form of tissue reactions. It is the most definitive criteria for defining different entities.
4. Clinical criteria: Easiest to apply as clinical features can be identified and applied easily.

Types

Madrid classification, Indian, New IAL, Ridley-Jopling, WHO classification

Table 1.1 Characteristics of Ridley-Jopling classification [3]

Parameters	TT	BT	BB	BL	LL
Number of lesions	1–3	<10	10–30	Many, asymmetrical (>30)	Numerous, symmetrical
Size of lesions	Large	Variable, some are large	Variable	Mostly small	Small
Surface	Dry and scaly	Dry and scaly, some looks bright and infiltrated	Dull/slightly shiny	Shiny	Shiny
Sensation	Absent	Diminished markedly	Moderately diminished	Slightly diminished	Minimally diminished, not affected
Hair growth in lesion	Absent	Diminished markedly	Moderately diminished	Slightly diminished	Not affected
AFB in lesion	Nil	Nil or scanty	Moderate	Many	Plenty includes globi
Lepromin reactivity	Strongly positive (+++)	Weakly positive (+/++)	Negative/ weakly positive	Negative	Negative

Ridley-Jopling Classification [1, 2]

Defined five groups on the basis of clinical, bacteriological, histological, and immunological features (Table 1.1). It is very useful in research purposes, but not feasible in primary health centers and field levels. This classification does not include indeterminate type and pure neuritic type of leprosy.

1. Tuberculoid leprosy (TT)
2. Borderline tuberculoid (BT)
3. Borderline borderline (BB)
4. Borderline lepromatous (BL)
5. Lepromatous leprosy (LL)

Indian Classification [4]

It includes six groups that have maculo-anesthetic (MA) and pure neuritic as separate categories. The main drawback was the classification was not entirely clinical and its usefulness at all levels of leprosy workers was doubtful. But it adds the pure neuritic leprosy cases which were not in Ridley-Jopling classification.

The types are as follows:

Lepromatous (L)
Tuberculoid (T)
Maculo-anesthetic (MA)
Polyneuritic (P)
Borderline (B)
Indeterminate (I)

New IAL Classification [5]

A modification of Indian classification has been adopted by IAL where maculo-anesthetic (MA) leprosy was merged with tuberculoid (T) leprosy.

Lepromatous (L)
Tuberculoid (T)
Polyneuritic (P)
Borderline (B)
Indeterminate (I)

WHO Classification (1988)

It was the most important classification of the disease for any treating leprologist. The patients were categorized depending upon whether slit skin smears demonstrate any bacilli or not.

Paucibacillary leprosy (PB): Only smear-negative cases and include indeterminate (I), tuberculoid (T), and borderline tuberculoid (BT) cases under Ridley-Jopling.

Multibacillary leprosy (MB): All smear-positive cases and mid-borderline (BB), borderline lepromatous (BL), and lepromatous (LL) types under Ridley-Jopling classification.

WHO Classification (1998) [6]

Application of slit skin smear universally to maintain their quality in control programs was the biggest challenge. Hence, in 1998, the WHO categorized PB and MB leprosy depending upon the number of skin lesions to overcome the operational problem of slit skin smear.

Paucibacillary single lesion leprosy (SLPB)
Paucibacillary leprosy (PB) (two to five skin lesions)
Multibacillary leprosy (MB) (six or more skin lesions and all smear-positive cases)

Table 1.2 WHO classification for field workers

Multibacillary (MB)	≥6 skin lesions, or positive bacterial index
Paucibacillary (PB)	≤5 skin lesions, or negative bacterial index

Table 1.3 NLEP classification

Characteristics	PB	MB
Skin lesions	One to five lesions (including single nerve lesion if present)	Six and above
Peripheral nerve involvement	No nerve/only one nerve with or without one to five lesions	More than one nerve irrespective of number of skin lesions
Skin smears	Negative at all sites	Positive at any site

Current WHO Classification

For field workers, the WHO has classified leprosy based on number of skin lesions for treatment purposes (Table 1.2). The sensitivity and specificity of this operational classification tested using slit skin smear and biopsy results as the gold standard were found to be 63% and 85%, respectively. 8th WHO expert excludes SLPB [7].

Classification Under NLEP, India (2009) [8]

This classification is currently used in India for treatment purposes. It considers the number of nerve involvement along with skin lesion count while categorizing PB and MB leprosy (Table 1.3). The main advantage includes early diagnosis of pure neuritic leprosy that constitutes around 4–5 percent of all leprosy cases in our country.

Conclusion

Not a single classification can only meet the expectations at all levels of leprosy workers. Currently, the WHO classification, based on skin/nerve lesion count, is simple and practical to follow for treatment purposes worldwide. Ridley-Jopling classification remains the most useful one for academic and research purposes.

References

1. Ridley DS, Jopling WH. A classification of leprosy for research purposes. Lepr Rev. 1962;33:119–28.
2. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five group system. Int J Lepr. 1966;34(3):255–73.
3. Kundu SK. Features of Ridley-Jopling classification and its application in the clinical field. Int J Lepr Other Mycobact Dis. 1979;47:64–5.
4. All India Leprosy Workers Conference. Classification of leprosy adopted by the Indian association of leprologists. Lepr India. 1955, 1955;(27):93–5.
5. Clinical, Histopathological. Immunological features of the five type classification approved by the Indian Association of Leprologists. Lepr India. 1982;54:22–32.
6. WHO. Expert committee on leprosy. 6th report. Geneva: World Health Organization; 1988. Tech Rep Ser 768.
7. World Health Organization. WHO expert committee on leprosy. 8th report. Geneva: WHO; 2012; No. 968.
8. World Health Organization, Leprosy Elimination Group. Guide to eliminate leprosy as a public health problem; WHO/CDS/CPE/2000.14. 2000. http//whqlibdoc.who.int/hq/2000/WHO_CDS_CPE_CEE_2000.14.pdf.

Chapter 2
Clinical Examination

Hemanta Kumar Kar and Mitanjali Sethy

Abstract Leprosy or Hansen's disease is caused by the Mycobacterium leprae (*M. leprae*) bacilli is a debilitating disease of the skin and peripheral nerves. It is a disease with five-district forms like localized tuberculoid (TT), Borderline tuberculoid (BT), Borderline Borderline (BB), Borderline lepromatous (BL) and the generalized lepromatous leprosy (LL). It presents with varied clinical manifestations, however skin lesions are usually the first sign noticed. Proper history taking and complete clinical examination helps in establishing the diagnosis of Leprosy. Many a time history and clinical examinations give clues to the spectrum of leprosy. Early and accurate diagnosis, and appropriate treatment are the key elements in preventing leprosy transmission and disabilities due to the disease.

Keywords Leprosy · Cutaneous examination · Peripheral nerve examination · Motor examination · Deformity

Introduction

Leprosy or Hansen's disease is a chronic infection caused by Mycobacterium leprae (*M. leprae*), an intracellular acid-fast bacillus, primarily a disease of skin and peripheral nerves. It manifests in different spectrums from localized tuberculoid (TT) to the generalized lepromatous leprosy (LL) passing through in between Borderline Tuberculoid (BT), Borderline (BB), Borderline lepromatous (BL) forms. In addition, there is one early type called Indeterminate Leprosy (IL) posing diagnostic dilemma clinically on many occasions before it terminates to any definite form described as above or disappears spontaneously. Sometimes in India, we encounter one definite type of leprosy called Primary Neuritic Leprosy (PNL) involving one or more peripheral nerves without any skin lesion. Later on, skin lesions may develop or may not appear at all. Therefore proper examination of skin,

H. K. Kar (✉) · M. Sethy
Kalinga Institute of Medical Sciences, KIIT University, Bhubaneswar, Odisha, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_2

peripheral nerves, and their cutaneous branches are very important for early and accurate diagnosis of leprosy because late recognition may give rise to deformities and disabilities development which is the main cause of stigma associated with leprosy [1].

Proper history taking and complete clinical examination help in establishing the diagnosis of Leprosy. Before examining the patient physically a complete history including the name, age, gender, occupation, address, present complaints, duration and evolution of lesions, past history, personal history, family history, and treatment history should be extracted from the patient. Sometimes a patient's history may not be very informative. Because of the slow and minimal progression of the disease, the patient may not remember what happened when. But many a time history gives clues to the diagnosis of the spectrum of leprosy. Based on the historical findings, the clinical examination should be conducted.

Clinical Examination

Clinical examination includes the following steps:

A. General examination
B. Cutaneous examination
C. Examination of peripheral nerves
D. Examination of musculoskeletal system
E. Mucosal examination
F. Genital examination
G. Other systemic examination

General Examination

A thorough general physical examination should be done to check pallor, icterus, edema, lymphadenopathy, pulse rate, blood pressure, temperature, and respiratory rate.

The general condition of the patient should be assessed. If the patient is acutely ill with fever, arthralgia, and myalgia, type 2 leprosy reaction (T2R) or severe type 1 leprosy reaction (T1R) should be suspected and cutaneous examination should be directed to confirm those. Many times such patients are referred from different departments like internal medicine, orthopedics, neurology, or rheumatology for exclusion of leprosy from a middle level or tertiary health care level set up and more often from primary health center (PHC) or community health center (CHC).

Pallor may be found in a patient due to leprosy who is on dapsone due to hemolysis, or even without due to multiple causes in India. Bilateral pedal edema is often seen in lepromatous leprosy patients, sudden onset of edema of hands and feet

suggestive of T1R, generalized edema, wide spread tender lymphadenopathy is associated with T2R [2]. Tachycardia may be noted in patients with reactions. Hypertension in patients with leprosy indicates chronic renal impairment due to repeated T2R or renal amyloidosis.

Cutaneous Examination

While doing the skin examination it is important that the patient should be stripped as far as possible to examine the entire skin surface, after ensuring privacy. It is preferable to examine the patient under direct sunlight. The patient should face the source of light while the examiner should sit/stand against it. The skin lesions are better appreciated in an oblique light (especially the ill-defined macules of LL disease), initially look at the skin from a distance and then close up to avoid missing pale patches [3].

A thorough inspection should be carried out to rule out diffuse fine and course cutaneous infiltration over the face, back, extensor aspects of upper and lower limbs, evident by shiny erythematous or brownish in dark skin, sparse body hair, prominent follicular openings. All the above skin features are indicative of early LL. Later on due to progressive nature of the disease, if remain undiagnosed and untreated, the ill-defined macules become diffuse infiltrative and already existing infiltrative skin becomes more thickened with appearance of papules, plaques and nodules, particularly on face with thick skinfolds and nodularity (leonine facies). Depressed nasal bridge, sparse beard, and moustache, unilateral or bilateral gynecomastia in males are to be meticulously checked. Diffuse brownish pigmentation of skin and conjunctiva indicates treatment with clofazimine, either currently or in the recent past [4].

While doing the cutaneous examination, the following points should be carefully looked for;

Number of Skin Lesions

Total number of skin lesions may be one or few or innumerable. The calculation of total number of skin lesions is required to classify the disease as paucibacillary or multibacillary.

The Distribution of Skin Lesions

To see whether the lesions are symmetrical or asymmetrical. Asymmetry in distribution indicates borderline spectrum of the disease and bilaterally symmetrical distribution indicates LL spectrum.

Examination of Individual Skin Lesion

Morphology

Macules/Patches/papules/plaques/nodules/vesicles/bulla/ulcer.

Size

Individual lesions may be small or large in the tuberculoid spectrum [TT (Fig. 2.1), BT] or they may be small and innumerable in BL and LL. Widespread innumerable ill-defined macules may coalesce to form diffuse infiltration, papules, nodules are suggestive of LL spectrum of disease (Fig. 2.2).

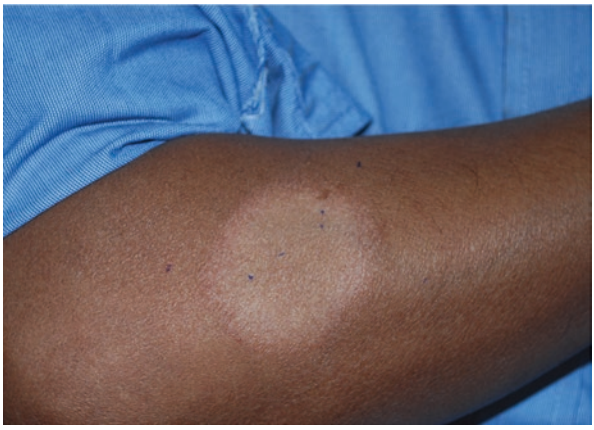

Fig. 2.1 Tuberculoid leprosy (TT) lesion with well-defined margin

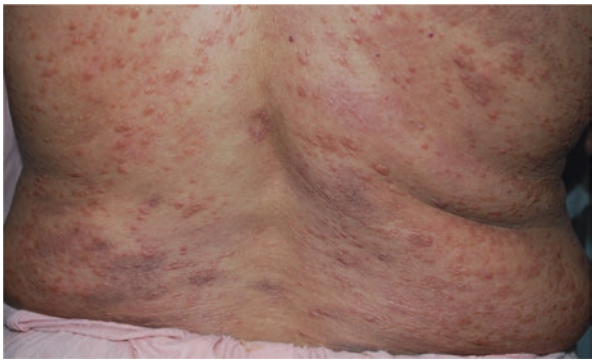

Fig. 2.2 Innumerable bilateral symmetrical papular and nodular skin lesions in LL

Shape

Regular (round/oval), irregular/bizarre, annular.

Margin/Edge of Skin Lesions

The margin (in flat lesions) and edge (in raised lesions) are well defined towards tuberculoid end (TT), partially or irregularly defined in BT lesions. Many times the edge is sloppier inwards in TT and BT and abrupt outwards and it is just opposite in BB called inverted saucer-shaped appearance (outer sloppy and inner abrupt). (Fig. 2.3a).

Satellite Lesions

Presence of pseudopodia and satellite lesions along the margins/edge of large lesions are suggestive of a BT lesion (Fig. 2.3b). Commonly these satellites lesions present near the irregular border of the primary lesions [5].

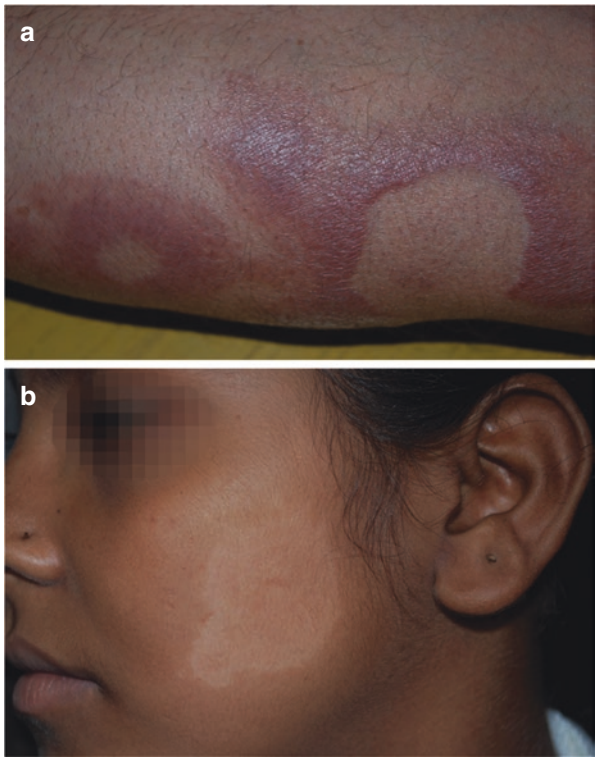

Fig. 2.3 (**a**) Inverted saucer-shaped (outer sloppy and inner abrupt margin) lesion in BB Leprosy. (**b**) Mark the satellite lesions in borderline tuberculoid leprosy lesion

Color of Lesion

Hypopigmented, coppery-red, skin-colored, or erythematous. During Type 1 Reaction (T1R) phase some or all of the old lesions may become reddish, swollen, and edematous. Fresh shiny and reddish new skin lesions may come up during T1R.

Surface

Dry (Fig. 2.4), scaly in TT/BT type, smooth and shiny in BB/BL types, edematous, ulcerated, necrotic in reaction phase of borderline spectrum. Look for presence/sparseness/absence of hair.

Tenderness

Tenderness over the existing lesions suggests T1R.

Anesthesia

Anesthesia is always present over the skin lesions in tuberculoid spectrum of leprosy, hypoesthesia (certain degree of impairment of sensation) on BT and BB skin lesions whereas no sensory loss observed over the lesions of lepromatous leprosy

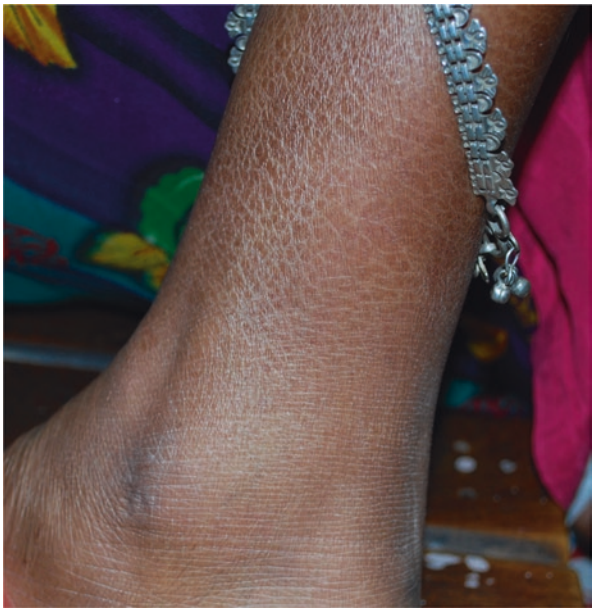

Fig. 2.4 Ichthyotic skin changes

[2]. However, due to bilateral peripheral nerve involvement, there will be glove and stocking type of anesthesia lately felt in LL. In the tuberculoid and borderline spectrum, in addition to sensory loss over the skin lesions, there may be loss of sensation over areas other than skin lesions supplied by the involved peripheral and cutaneous nerve.

Touch sensation using a wisp of cotton-wool or nylon monofilaments, pain sensation through pinpricks, temperature sensation using hot/cold water in test tubes should be performed. Before eliciting the sensation tests, first explain to the patient what you will be doing properly. After he/she understands, fully demonstrate the procedure while he watches with the eye open and points exactly the spot touched. Then continue the testing on various sites while the patient's eye is closed. While testing sensation, the examiner should proceed from uninvolved to the involved skin and he should touch the area gently and shouldn't brush across the skin. If the patient is unable to identify the spots stimulated indicates anesthesia. If he feels it but cannot touch the exact point, it is called 'misreference' which is the earliest sign of hypoesthesia. The normal range of accuracy on the hand is within 1 cm, the face 2 cm, and up to 7 cm on the back and buttocks [2]. Hypoesthesia can be detected when the patient feels less skin lesion than the corresponding area on the other side of the body.

The WHO recommends sensory testing sites on palms and soles (10 sites on each side) for disability grading (Fig. 2.5) [6]. Sensory innervation of palm and sole has been shown in Figs. 2.6 and 2.7 respectively.

The signs of autonomic nerve damage are loss of sweating, which is shown by dryness, callosities, and fissuring in the patient. In case of doubtful lesions, anhidrosis can be detected by ninhydrin test or pilocarpine test [7, 8].

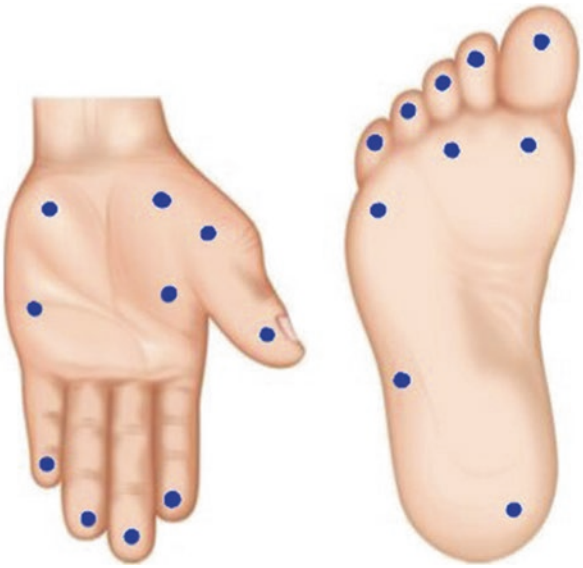

Fig. 2.5 Recommended sensory testing sites (WHO) on palms and soles

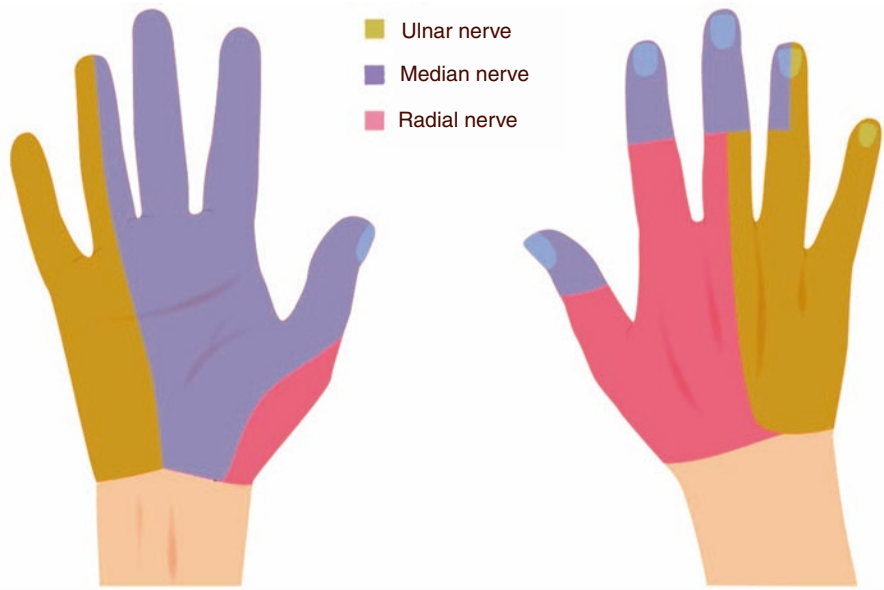

Fig. 2.6 Sensory innervation of palm

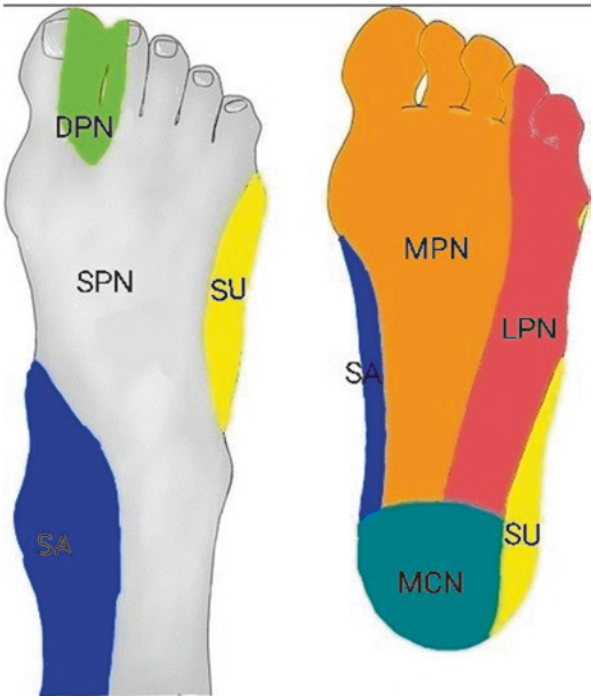

Fig. 2.7 Sensory innervation of sole. (Abbreviations: *SA* saphenous nerve, *SU* sural nerve, *DPN* deep peroneal nerve, *SPN* superficial peroneal nerve, *MPN* medial plantar nerve, *LPN* lateral plantar nerve)

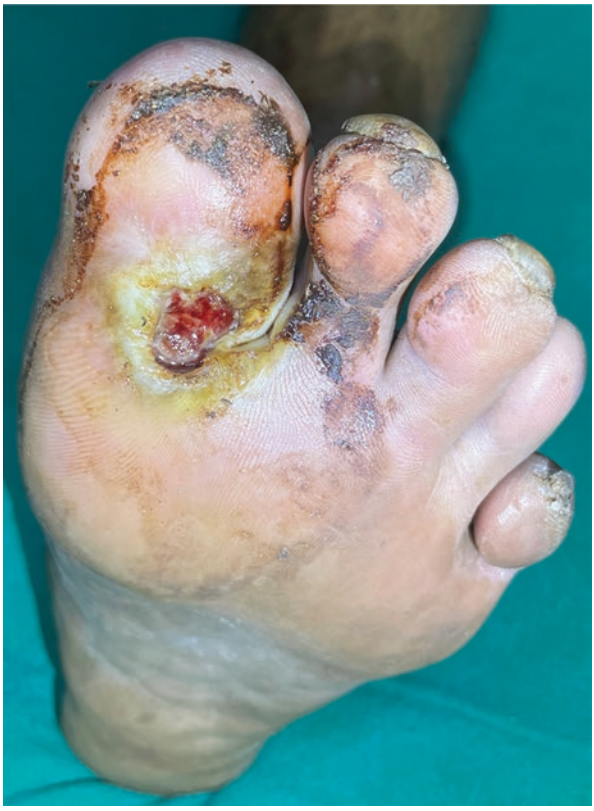

Fig. 2.8 Trophic ulcer

Trophic ulcer (Fig. 2.8) if present should be examined for evidence of secondary bacterial infections such as discharge, foul smell, and dirty slough.

Examination of Peripheral Nerves

The cutaneous nerves can be palpated near the skin lesions, especially around the plaques of TT/BT leprosy. However, certain peripheral nerves are commonly affected in leprosy at certain sites and can be palpated at those sites. The sites of predilection at which peripheral nerves are most commonly enlarged and palpable in leprosy have been shown in Fig. 2.9.

The common peripheral nerves affected are Ulnar, Median, Radial, Cutaneous branch of the radial, Common peroneal, Posterior tibial, Great auricular nerve, Supraorbital, and Supra trochlear nerve. Before palpating the peripheral nerves few points should be kept in mind such as; [4].

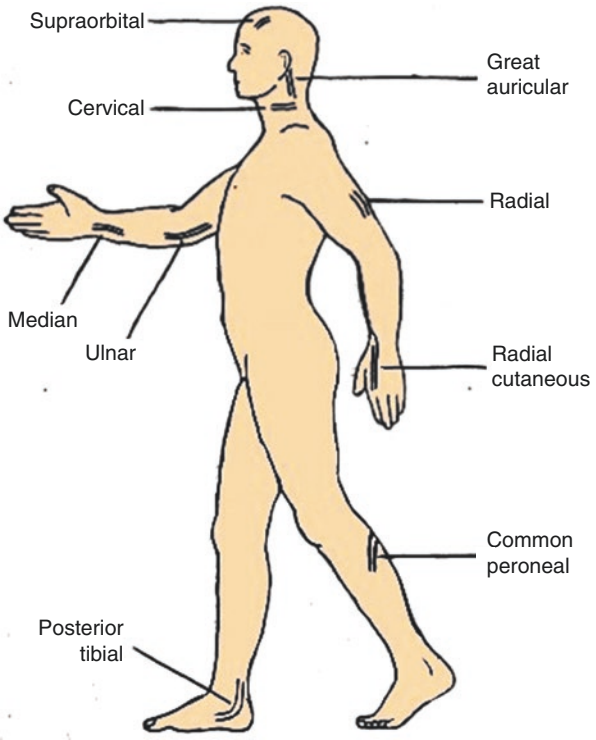

Fig. 2.9 The sites of predilection at which peripheral nerves are most commonly enlarged and palpable in leprosy

1. Nerves should be palpated gently (pulp of the finger should be used instead of fingertip) without hurting the patient.
2. Tender or not? As the nerves are being palpated the examiner should look at the patient's face. The patient will wince if they are tender. Neuritis is much more common in T1R.
3. Nerve is palpable or not? Large peripheral nerve trunks are usually not palpable in the indeterminate and TT spectrum of the disease.
4. If the nerve is palpable, then whether it is unilateral or bilateral? Each nerve should be palpated on both sides for comparison. Asymmetry in nerve enlargement is a feature of the borderline spectrum of leprosy.
5. Extent of the nerve thickness in its course.
6. Look for consistency of the nerve.
7. Presence of any abscess or nodularity (fusiform, diffuse swelling).
8. Presence of any tingling sensation along the nerve course.

The method of peripheral nerve examination has been described below [4].

Nerve	Method of examination
Ulnar nerve (Fig. 2.10)	The patient should face the examiner and sit or stand with the elbow flexed at 90°. To examine the right ulnar nerve, the examiner should hold the right hand of the patient. With the left hand little finger, he will locate the nerve in the ulnar groove (olecranon groove) on the medial epicondyle of humerus and with other fingers, and he will palpate the nerve upward along the medial aspect of the arm.
Radial nerve (Fig. 2.11)	The position of the patient will be the same as that of ulnar nerve palpation. To examine the right radial nerve, the examiner will roll the nerve in the spiral groove on the humerus, posterior to the deltoid insertion with left-hand fingers.
Median nerve (Fig. 2.12)	The examiner should hold the wrist of the patient in supination. To examine the right median nerve, the examiner should hold the patient's right hand with his left hand. With right hand fingers, he will roll across the center of the wrist. The enlarged nerve can be palpated proximal to the wrist under the palmaris longus tendon.
Radial cutaneous nerve (Fig. 2.13)	Patient is asked to extend the thumb to make the anatomical snuffbox visible. The examiner can roll the nerve against the lateral border of radius just proximal to the wrist.
Lateral popliteal nerve (Fig. 2.14)	Patient is asked to sit with legs hanging freely. The examiner should stabilize the knee by placing his thumbs on the upper border of patella on both sides and the nerve can be rolled with the pulp of fingers, against the neck of the fibula.
Sural nerve (Fig. 2.15)	The patient is asked to be in a standing or prone position. The nerve to be palpated in the posterior aspect of leg, between the two bellies of gastrocnemius above and tendo-achilles below.
Posterior tibial nerve (Fig. 2.16)	The patient should be standing or sitting on bed with knee flexed. The nerve can be palpated by rolling the fingers in the medial aspect of the ankle (deep to flexor retinaculum) posterior and inferior to the medial malleolus.
Anterior tibial nerve	Patient is asked to sit on bed with legs straight and extend the great toe to make the extensor hallucis longus tendon standout. The nerve can be palpated by rolling fingers on the dorsum of foot, lateral to the tendon of extensor hallucis longus and dorsalis pedis artery.
Supraorbital nerve (Fig. 2.17)	The patient should face the examiner in a standing or sitting position. Run the thumbs across the forehead from the midline laterally. The nerve can be palpated in the supraorbital notch at the junction of medial one-third and lateral two-thirds of supraorbital ridge.
Supratrochlear nerve	It is to be palpated medial to the supraorbital nerve
Infraorbital nerve	The nerve can be palpated in the infraorbital foramen, just below the medial part of inferior orbital margin.
Great auricular nerve (Fig. 2.18)	The nerve is easily visible across the sternomastoid muscle when the head is turned to the opposite side. May be palpated with fingers on the lateral side of the neck crossing the sternomastoid muscle.
Clavicular nerves	Clavicular nerves can be palpated along the shafts of both clavicles.

Fig. 2.10 Examination of ulnar nerve

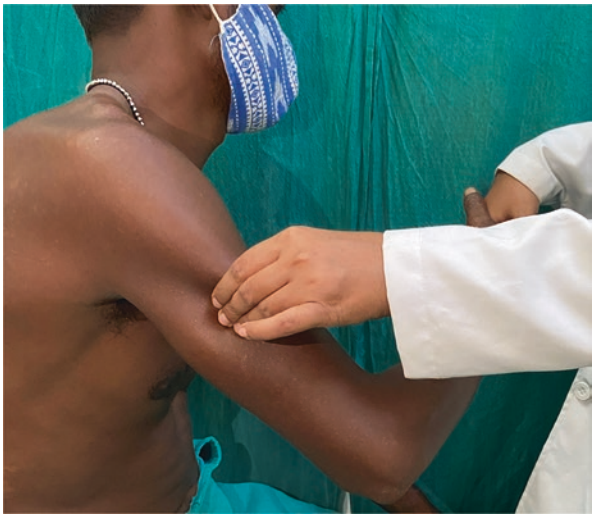

Fig. 2.11 Examination of radial nerve

Fig. 2.12 Examination of median nerve

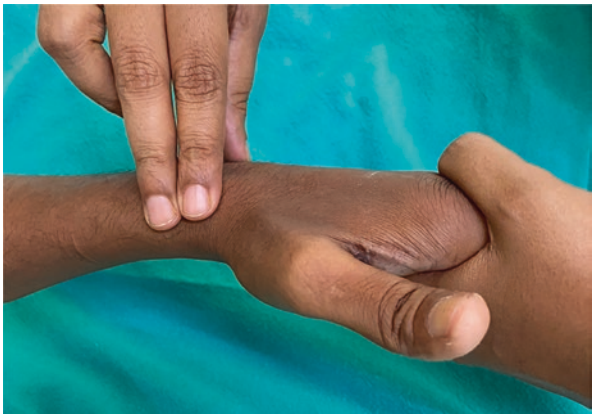

Fig. 2.13 Examination of radial cutaneous nerve

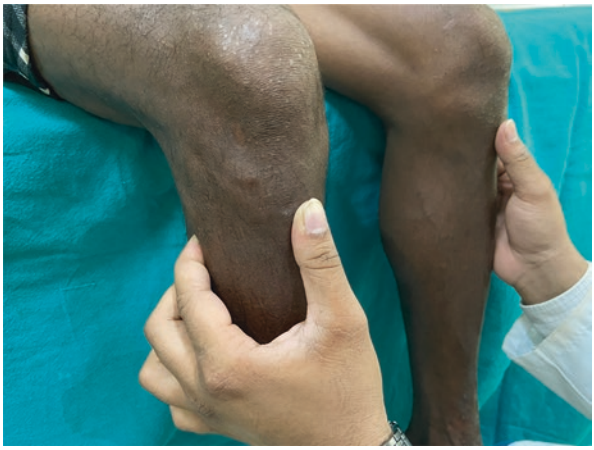

Fig. 2.14 Examination of lateral popliteal nerve

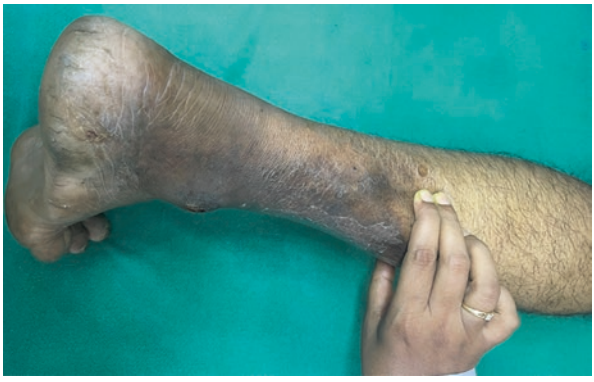

Fig. 2.15 Examination of sural nerve

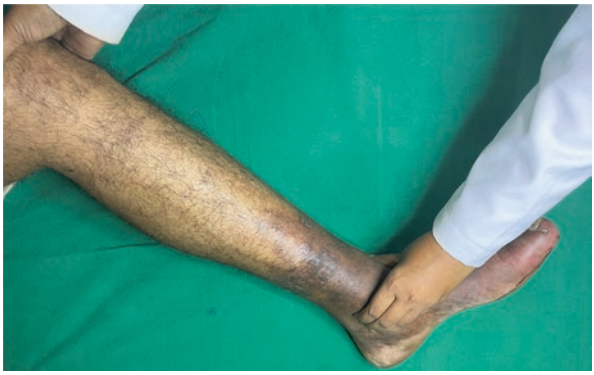

Fig. 2.16 Examination of posterior tibial nerve

Fig. 2.17 Examination of supraorbital nerve

Examination of Musculoskeletal System

Detailed examination of the musculoskeletal system should be done for a definite diagnosis of leprosy. Before going to the motor examination proper a thorough inspection should be carried out to find any deformity like collapse of the ridge of nose (destruction of anterior nasal spine), destruction of ala nasi, loss of upper incisor teeth, wrist drop, claw hand, gait abnormality (high stepping gait), foot drop and claw toes.

Motor Examination

During motor examination, certain things should be carefully looked at such as if there are any difficulties in walking or in using hands, deformity, any other signs of muscle weakness, paralysis, or wasting. Functions of the muscles of the forearm,

Fig. 2.18 Examination of great auricular nerve

hand, leg, and feet are assessed by certain tests like voluntary muscle testing (VMT). The six grades for VMT [Medical Research Council (MRC) scale] in higher centers are as follows: [9].

- *Grade0*: No movement is observed.
- *Grade1*: Flicker of movement or fasciculation are observed.
- *Grade2*: Active movement when the resistance of gravity is eliminated.
- *Grade3*: Muscle strength is reduced but movement possible without resistance.
- *Grade4*: Muscle strength is reduced but muscle contraction against slight resistance.
- *Grade5*: Normal power (muscle contracts normally against full resistance).

Muscle Strength Grading in Peripheral Centers

- Strong (S): when the movement is normal and strength seems normal.
- Weak (W): when the muscle can move but it is definitely weak against resistance.
- Paralyzed (P): when there is no movement at all.

Methods of muscle testing, suggested by different authors have been presented in the following Table 2.1.

Table 2.1 Testing of muscles of the hand

Nerve	Muscle	Test	Interpretation	Disability/deformity
Ulnar				
	Dorsal interossei	*Little finger out test:* Ask the patient to spread the little finger out while the examiner applies resistance at the base of the little finger. *Egawa's test:* All fingers tested for abduction against resistance.	Inability to do so	Guttering of interosseous spaces
	Adductor pollicis and first palmar interossei	*Book test:* Ask the patient to hold a book between two hands by keeping the adducted thumbs straight on its upper surface against resistance. (Fig. 2.19)	*Froment's sign:* Flexion of the distal inter-phalangeal joint of thumb with hyperextension of MCP joint on affected side indicates weakness of these two muscles	Guttering of first interosseous space
	Interossei and medial two lumbricals	Patient asked to flex the fingers at MCP joints against resistance	Inability to do so indicates weakness of these two groups of muscles	*Claw hand*; (Fig. 2.20) hyperextension at MCP and flexion at IP joints
	Palmar interossei	*Card test:* (Fig. 2.21) Ask the patient to keep fingers extended and adducted. A firm paper card is inserted in each web-space and the patient is instructed to grasp it tightly while the examiner will try to pull it out.	Inability to do so indicates weakness of palmar interossei	Mild guttering of interosseous spaces *Wartberg's sign:* Subtle abducted position of little finger earliest sign of ulnar nerve involvement

Table 2.1 (continued)

Nerve	Muscle	Test	Interpretation	Disability/deformity
Median nerve				
	Abductor pollicis brevis	*Pen test:* (Fig. 2.22) Ask the patient to lay his hand flat with palmar surface upon a table and ask him to touch a pen held slightly higher, by moving the thumb vertically up (abduction).	Inability to do so indicates loss of abduction movement of thumb	*Ape-thumb deformity*: Thumb lies flat in the same plane of hand (adducted, hyperextended and rotated at carpometacarpal joint and flexed at MCP and IP joints.
	Opponens pollicis	Examiner will stabilize the patient's hand with his hand and the patient is asked to touch the tips of other fingers with thumb while the examiner is resisting this action with his index finger.	Inability to do so indicates weakness of opponens pollicis	
	Flexor digitorum superficialis and flexor digitorum profundus (lateral half)	*Ochsner's clasping test:* (Fig. 2.23) Ask the patient to clasp both hands.	Index finger of affected side remains straight and does not flex	*Pointing index/ benediction sign* Outstretched index finger with flexion of other fingers
Radial nerve				
	Extensors of wrist joint	Close fist and dorsiflex the wrist joint against resistance	Inability to do so	Wrist drop
Test for all 3 nerves of one hand		*Beak test:* (Fig. 2.24) Ask the patient to shape his fingers like a beak and move the hand to and fro at the wrist joint	If he can do so, all 3 nerves of the hand are healthy	

(continued)

Table 2.1 (continued)

Nerve	Muscle	Test	Interpretation	Disability/deformity
Testing of muscles of the foot				
Common peroneal nerve/lateral popliteal nerve	Dorsiflexors of ankle, extensor hallucis longus, tibialis anterior	Ask the patient to perform dorsiflexion at ankle, extension of great toe, eversion of foot against resistance by examiner's hand	Inability to do so indicates weakness of these muscles	Foot drop
Medial and lateral plantar branches of tibial nerve	Intrinsic muscles of feet	Ask the patient to place foot firmly on the ground and lift toes and spread them out	Inability indicates weakness of these muscles	Guttering of intertarsal spaces Clawing of toes
Testing muscles of the face				
Zygomatic and temporal branches of facial nerve	Orbicularis oculi	Ask the patient to close the eyes forcefully and examiner tries to separate the eyelids	Unable to keep the eyelids closed indicates weakness of the muscle	Lagophthalmos

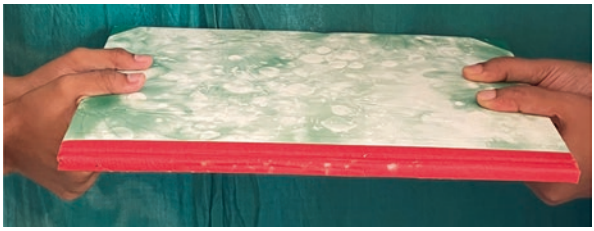

Fig. 2.19 Book test

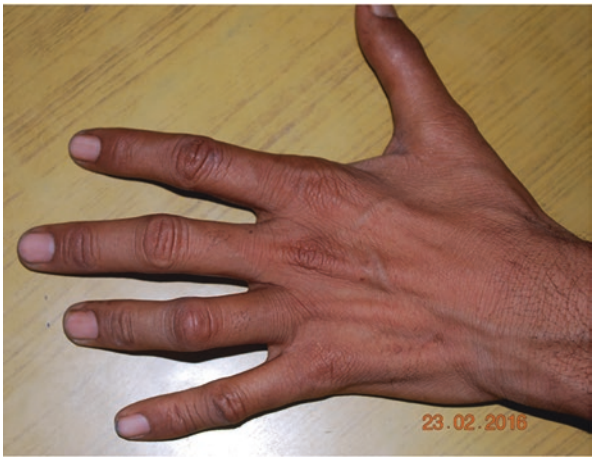

Fig. 2.20 Partial claw hand with atrophy of muscles

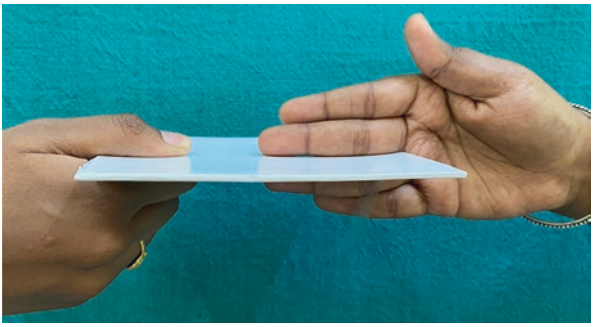

Fig. 2.21 Card test

Fig. 2.22 Pen test

Mucosal Examination

Examination of mucosa in leprosy clinics is often neglected. Meticulous examination of nasal, ocular and oral mucosa often gives clues to the definite diagnosis of leprosy.

Nasal Mucosa Examination

Look for crusts, bleeding from nose and septal perforation.

Fig. 2.23 Ochsner's clasping test with pointing index

Fig. 2.24 Beak test

Oral Mucosa Examination

Oral cavity involvement more common in multibacillary leprosy compared with paucibacillary disease [10]. Diffuse enlargement of lips, nodular lesions over the anterior part of the tongue, giving a pavement-stone appearance, swollen uvula, involvement of gums in the form of gingivitis, periodontitis and periodontoclasia may occur in leprosy [11].

Ocular Examination

Look for width of the palpebral fissure, frequency of blinking, loss of or sparse eyebrow (Fig. 2.25), loss of eyelashes, trichiasis, redness of eyes, and pterygium [12].

Fig. 2.25 Loss of eyebrows. Courtesy: Dr. Piyush Kumar, Madhubani Medical College and Hospital, India

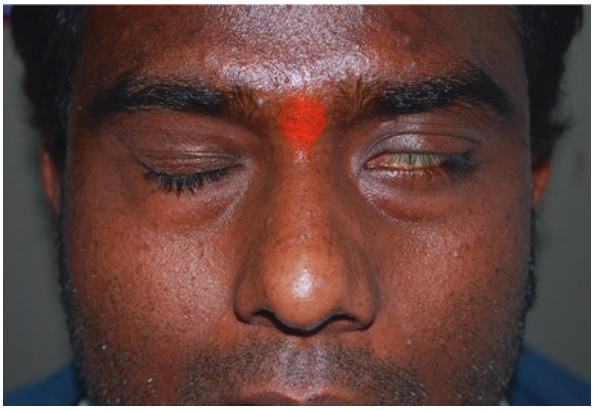

Fig. 2.26 Lagophthalmos

Test for Lagophthalmos

Ask the patient to close the eyes and if there is a space between the upper and lower eyelid margins, is suggestive of lid retraction or lagophthalmos (Figs. 2.26 and 2.27).

Ask the patient to look straight. The examiner will approach the patient from one side and touch the cornea, 2 mm inside the limbus at the 6 o'clock position gently with a clean wisp of cotton-wool. Normally there should be a brisk blink response [13]. Unilateral absence of corneal reflex may be because of involvement of ophthalmic nerve (trigeminal) due to a same sided BT lesion around eye. Bilateral loss of corneal reflex indicates damage to corneal nerves that may be due to advanced LL disease [2].

Fig. 2.27 Test for corneal sensation

External Genital Examination

In the case of male patient, examine the testis for size and consistency, tenderness, and testicular sensation.

Other Systemic Examination

The lymph-nodes, internal organs like liver, kidney, larynx, and joints are usually involved in lepromatous leprosy and T2R.

Conclusion

The principle of leprosy control is based on early detection of all cases and treatment with multidrug therapy thereby preventing the deformities and stigma in the community. For achieving zero leprosy in the glove, early detection of all cases is of paramount importance. A lot of information can be collected from the proper history taking and clinical examinations. The primary objective of clinical examination is to elicit cardinal signs of leprosy through a thorough systemic examination. Sensory testing, examination of peripheral nerves, and examination of muscles help clinicians to arrive not only early diagnosis of leprosy, but also for prevention of deformities through a timely initiation of specific therapy.

References

1. Belachew WA, Naafs B. Position statement: LEPROSY: diagnosis, treatment and follow-up. J Eur Acad Dermatology Venereol. 2019;33(7):1205–13.
2. Pfaltzgraff RE, Ramu G. Clinical leprosy. In: Hastings RC, Diltor VAO, editors. Leprosy. 2nd ed. Edinburgh: Chuchill Livingstone; 1994. p. 237–86.
3. Bryceson ADM, Pfaltzgraff RE. Symptoms and signs. In: Bryceson ADM, Pfaltzgraff RE, editors. Leprosy. 3rd ed; 1990. p. 25–54.
4. Palit A, Ragunatha S, Inamadar AC. History taking and clinical examination. In: Kumar B, Kar H, editors. IAL textbook of leprosy. 2nd ed. Jaypee Brothers Medical Publishers; 2016. p. 207–35.
5. Jopling WH, Mc Dougall AC. The disease. In: Jopling WH, Dougall M, editors. Handbook of leprosy. 5th ed. CBS Publishers and Distributors; 1996. p. 10–53.
6. Brandsma JW, Van Brakel WH. WHO disability grading: operational definitions. Lepr Rev. 2003;74(4):366–73.
7. Chattopadhyay SP, Borua PC, Rathore BS. Value of pilocarpine test in early diagnosis of leprosy. Indian J Lepr. 1984;56(4):877–83.
8. Markendeya N, Srinivas CR. Ninhydrin sweat test in leprosy. Indian J Lepr. 2004;76(4):299–304.
9. Pearson JM. The evaluation of nerve damage in leprosy. Lepr Rev. 1982;53(2):119–30.
10. Morgado de Abreu MAM, de Avelar M, Alchorne M, Michalany NS, Weckx LLM, Pimentel DRN, Hirata CHW. The oral mucosa in paucibacillary leprosy: a clinical and histopathological study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103(5):e48–52.
11. Kaur A, Pallagatti S, Sheikh S, Singh R, Aggarwal A. Oral cavity and leprosy. Indian Dermatol Online J. 2012;3(2):101.
12. Lamba PA, Kumar DS. Ocular involvement from leprosy. Indian J Ophthalmol. 1984;32(2):61–3.
13. Daniel E. Lagophthalmos in leprosy. Indian J Lepr. 1998;70:39–47.

Chapter 3
Microbiological Investigations and Histopathology

Sasi Attili, Hiral Shah, and Piyush Kumar

Abstract The diagnosis of leprosy requires demonstration of lepra bacilli. Slit skin smear and stain are helpful in diagnosing multibacillary cases. In paucibacillary cases, where the bacterial load is low and demonstrating lepra bacilli is very difficult, biopsy may be helpful in establishing the diagnosis. Tuberculoid leprosy shows epithelioid granuloma, usually centered on the nerves and the appendages. Lepromatous leprosy is characterized by diffuse infiltration of the dermis with foamy histiocytes laden with plenty of bacilli. The histopathology of histoid leprosy is distinctive, and spindle-shaped histiocytes arranged in bands or whorls are seen.

Keywords Leprosy · Histopathology · Granuloma · Epithelioid granuloma · Langhans giant cell · Foamy histiocytes

Introduction

The "gold standard" for the diagnosis of an infectious condition is demonstration and culture of the microorganism. *M. leprae* is usually not identified in paucibacillary cases and is not cultivable. The search for another diagnostic tool is fulfilled by histopathology which not only provides enough diagnostic clues but also helps in classifying the disease as per five-part Ridley-Jopling classification. Slit skin smear is a fact technique to demonstrate acid-fast bacilli (AFB), but its usefulness is limited in clinical practice.

S. Attili
Visakha Institute Of Skin & Allergy, Vizag, India

H. Shah
Baroda Medical College, Vadodara, India

P. Kumar (✉)
Dermatology Venereology and Leprosy, Madhubani Medical College and Hospital, Madhubani, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_3

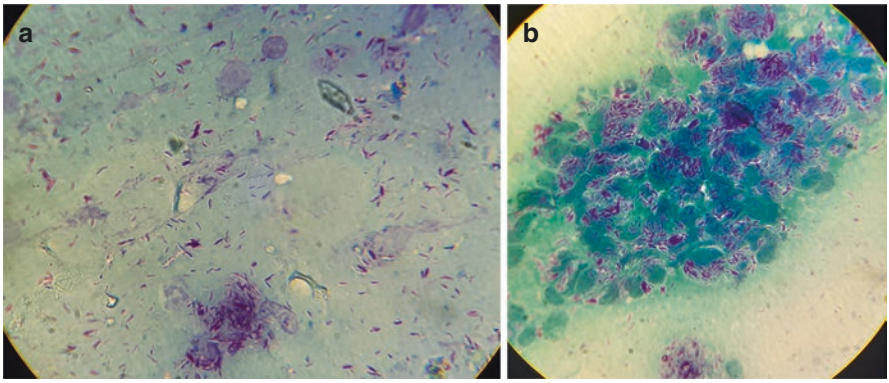

Fig. 3.1 (**a**) *M. leprae* is seen as rod-shaped, bright red colored bacilli (Ziehl-Neelsen, ×1000). (**b**) Clumps of *M. leprae* (globi) (Ziehl-Neelsen, ×1000)

Slit Skin Smear (SSS) [1, 2]

- Tissue fluid from the skin lesion and sites with expected high bacterial load (e.g., earlobe) is taken on a glass slide and is dried and stained with Ziehl-Neelsen stain or Fite stain (Fig. 3.1a, b).
- The number of bacteria is counted under light microscopy at high magnification with oil immersion, and the bacterial index is calculated as per Ridley's logarithmic scale.
- The sensitivity and, hence, diagnostic usefulness depend on the bacterial load and are low in paucibacillary cases.
- Hence, the clinical utility of SSS is limited, as SSS will be positive in multibacillary cases where clinical diagnosis itself is obvious, but it would not help in paucibacillary cases where clinical diagnosis is doubtful and requires diagnostic support.

Histopathology

For diagnostic purposes, deep biopsy including the complete dermis from the most active part of lesion should be obtained. Tuberculoid leprosy is characterized by well-formed granulomas, often perineural in location and assuming a serpentine shape. On the other hand, in the lepromatous spectrum, there is a diffuse infiltration of histiocytes laden with bacilli throughout the dermis, sparing the upper papillary dermis (grenz zone). However, in several cases, the clinical features do not correlate with the histological findings. Clinically, tuberculoid lesions may show lepromatous features histologically, and vice versa. Further the histological features and

Table 3.1 Histopathological classification of leprosy

	TT	BT	BB	BL	LL
Grenz zone	–	+	+	+	+
Epithelioid granuloma	+++ (well formed)	++ (less well developed)	± (variable)	–	–
Foamy macrophages	–	–	–	++ (focal/ nodular)	+++ (diffuse)
Location of granuloma	Perineural, perivascular	Perineural, perivascular, periappendageal	Perivascular	Perivascular	Diffuse
Langhans giant cells	+++ (large well developed)	++ (smaller)	±	Rare	–
Lymphocytes	+++ (periphery of granuloma)	+ (within granuloma, when present)	+	++ (seen throughout the macrophage granuloma)	+ (focal aggregates)
Acid-fast bacilli (AFB)	±	±	+	++	+++ (Globi)

bacteriological index may vary from lesion to lesion, even within the same patient. Clinicopathological correlation is essential. The salient features of different poles of leprosy are summarized in Table 3.1 and are discussed below. While H&E stain provides details of infiltration and architectural changes, bacilli are visualized on Wade-Fite stain or Fite-Faraco stain [3, 4].

The salient histopathological features of leprosy are discussed below [5, 6, 7].

Tuberculoid Leprosy (TT)

- Multiple, well-formed, noncaseating granulomas in the dermis rimmed by lymphocytes.
- Granulomas are composed of epithelioid histiocytes and some multinucleate Langhans giant cells (Fig. 3.2a–c).
- Caseous necrosis is rare but may be seen in granulomas involving the nerve.
- Granulomas originate in perineural locations and expand to involve other areas.
- No grenz zone. Granulomas may erode the undersurface of the epidermis.
- AFB not seen.
- When visualization of nerves on H&E staining is difficult, S-100 immunostaining would help.
- Granulomas may extend to and damage arrector pili muscles, hair follicles, and sweat glands.

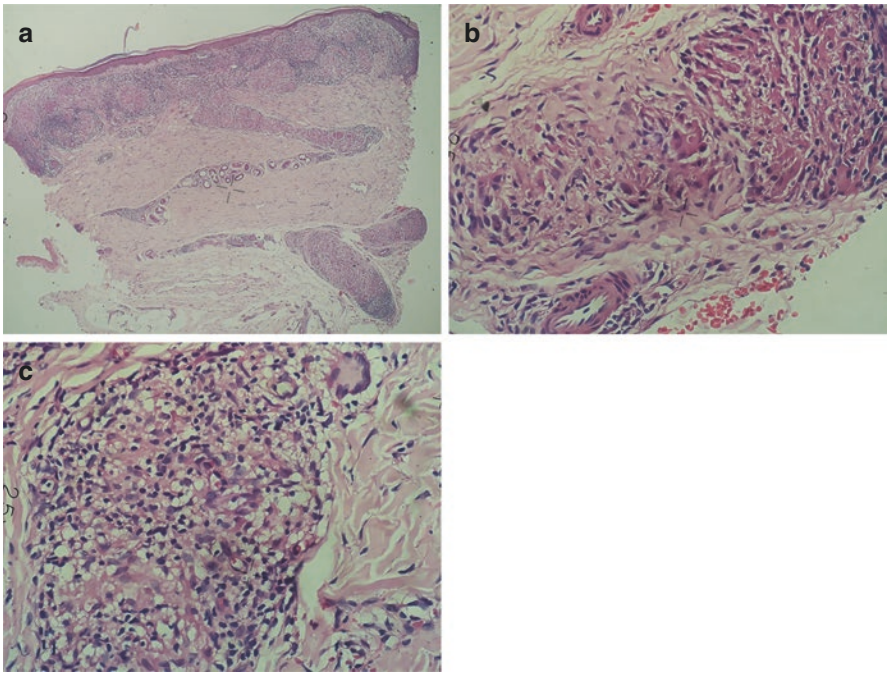

Fig. 3.2 (**a**) Epidermal thinning with well-formed epithelioid granuloma (H&E ×100). (**b**) Well-formed, elongated epithelioid granuloma (H&E ×400). (**c**) Langhans giant cell, histiocytes, and epithelioid cells in granuloma (H&E ×400)

Borderline Tuberculoid Leprosy

- Grenz zone seen (Fig. 3.3a–c).
- Well-formed granulomas.
- Lymphocytes are less than those in TT.
- Swollen nerve bundle may be identified within the granuloma.
- BI is 0–2+.

Borderline Leprosy

- Epithelioid cells present in a diffuse manner.
- Lymphocytes are present diffusely.
- Langhans giant cells usually not present.
- Nerve bundles identified—Schwann cell proliferation. Perineural fibrosis may be noted.
- BI is 2–3+.

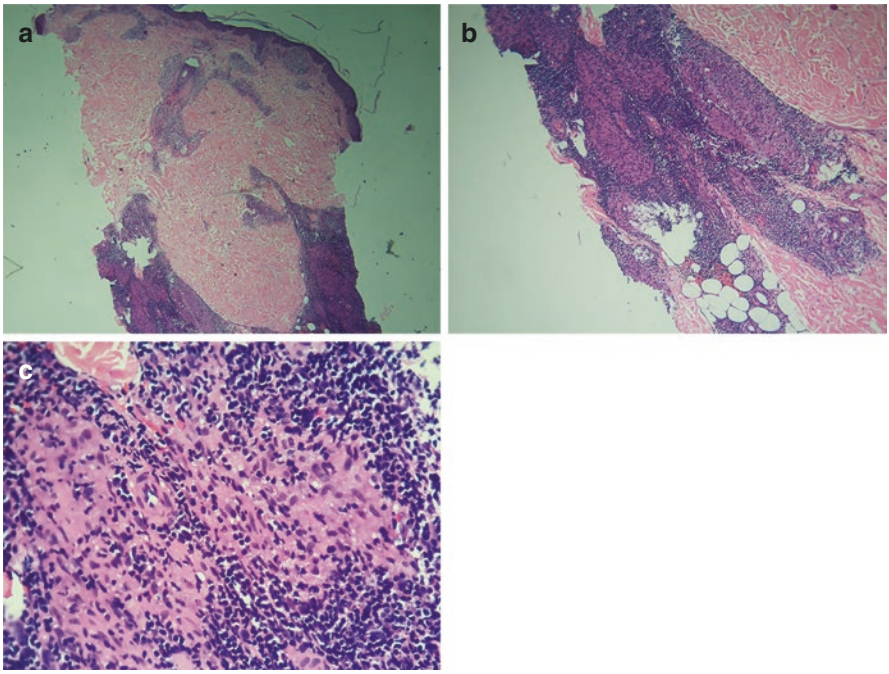

Fig. 3.3 (**a**) Epidermal thinning, grenz zone, and well-formed granuloma reaching up to deeper dermis (H&E ×100). (**b**) Oblong-shaped well-formed granuloma with lymphocytes at the margin (H&E ×400). (**c**) Well-formed granuloma with histiocytes and epithelioid cells in the center and lymphocytes at the margin (H&E ×400)

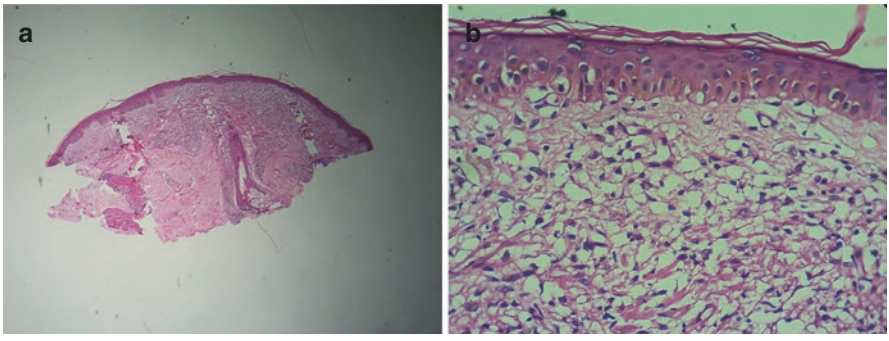

Fig. 3.4 (**a**) Foamy macrophages infiltrating the dermis (H&E ×100). (**b**) Sheets of foamy macrophages (H&E ×400)

Borderline Lepromatous Leprosy

- Foamy macrophages with granular cytoplasm diffusely present (Fig. 3.4a, b).
- Lymphocytes variable—present around the nerves.
- Grenz zone.
- BI is 2–4+.

Lepromatous Leprosy

- Grenz zone.
- Sheets of foamy histiocytes containing numerous AFB. Globi seen. Presence of numerous bacilli gives a grayish tinge to the cytoplasm on H&E stain (Fig. 3.5a–c).
- Nerve bundles lack cellular infiltrate but may show damage.
- BI 5+.

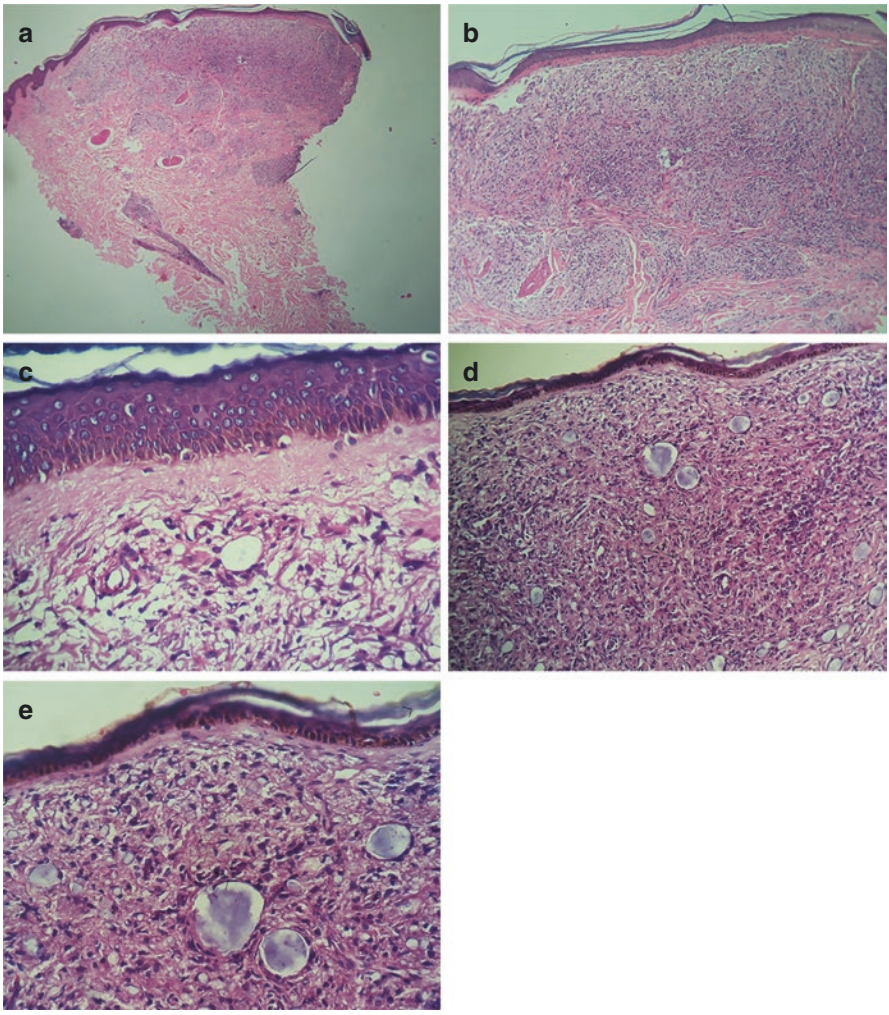

Fig. 3.5 (**a**) Grenz zone and foamy macrophages in the upper and mid dermis (H&E ×40). (**b**) Foamy macrophages with interspersed lymphocytes (H&E ×100). (**c**) Higher magnification (H&E ×400). (**d**) Rarely, acid-fast lepra bacilli seen as blue-gray intracytoplasmic mass (H&E ×400). (**e**) Higher magnification (H&E ×400)

Indeterminate Leprosy

- Sparsely perivascular, perineural, and periadnexal infiltrate of lymphocytes and a few histiocytes.
- Bacilli are usually absent. AFB may be found when a dermal nerve is followed on serial sections.

Histoid Leprosy

- Atrophic epidermis.
- Grenz zone may be seen.
- Circumscribed nodular mass in the dermis consisting of spindle cells filled with bacilli. Cells are arranged in a storiform pattern. Central necrosis may be seen.
- Pseudocapsule may be noted.

Pure Neural Leprosy

- Epithelioid granulomas, mononuclear cell infiltrate, perineural/subperineural edema, fibrosis, and a decrease in myelinated fibers.
- Immunohistochemistry using antibodies against lipoarabinomannan and phenolic glycolipid 1 (PGL-1).

Type 1 Reaction

Upgrading Reaction

- Granulomatous destruction of the nerves and dermal edema.
- Increased granulomatous organization, increased lymphocytes, and an increased number of multinucleated giant cells.

Downgrading Reaction

- Macrophages replace lymphocytes and epithelioid cells.

Type 2 Reaction (Erythema Nodosum Leprosum)

- Superimposed upon the chronic inflammation of lepromatous leprosy.
- Dermal neutrophils with vasculitis.
- In older lesions, neutrophils may not be found.
- Predominantly lobular panniculitis may be noted.

Resolution [8]

Resolution of histopathological changes in leprosy is seen after treatment or, sometimes, even without treatment. The fate however differs in tuberculoid and lepromatous poles.

- In tuberculoid poles, the granuloma usually disappears within a year. Nonspecific lymphocytic infiltration may be the only residual change.
- In lepromatous lesions, degenerative changes cause lipid accumulation, reflecting as foamy changes. These foamy residues resolve very slowly and may persist for years.

References

1. Banerjee S, Biswas N, Kanti Das N, Sil A, Ghosh P, Hasanoor Raja AH, Dasgupta S, Kanti Datta P, Bhattacharya B. Diagnosing leprosy: revisiting the role of the slit-skin smear with critical analysis of the applicability of polymerase chain reaction in diagnosis. Int J Dermatol. 2011;50(12):1522–7.
2. Mahajan VK. Slit-skin smear in leprosy: lest we forget it! Indian J Lepr. 2013;85(4):177–83.
3. Chan MMF, Smoller BR. Overview of the histopathology and other laboratory investigations in leprosy. Curr Trop Med Rep. 2016;3:131–7.
4. Lastória JC, Abreu MA. Leprosy: a review of laboratory and therapeutic aspects–part 2. An Bras Dermatol. 2014;89(3):389–401.
5. Maymone MBC, Laughter M, Venkatesh S, Dacso MM, Rao PN, Stryjewska BM, Hugh J, Dellavalle RP, Dunnick CA. Leprosy: clinical aspects and diagnostic techniques. J Am Acad Dermatol. 2020;83(1):1–14.
6. Singh A, Weng X, Nath I. Skin biopsy in leprosy. In: Khopkar U, editor. Skin biopsy-perspectives. Intech Open; 2011. p. 73–86. https://www.intechopen.com/chapters/22583.
7. Scollard DM. Pathogenesis and pathology of leprosy. In: Scollard DM, Gillis T, editors. International textbook of leprosy; 2017. https://internationaltextbookofleprosy.org/chapter/pathology.
8. Joshi R. Clues to histopathological diagnosis of treated leprosy. Indian J Dermatol. 2011;56(5):505–9.

Chapter 4
Electrophysiological and Radiological Investigations

Malcolm Pinto and M. Manjunath Shenoy

Abstract Leprosy is an important chronic, infectious disease affecting the peripheral nerves. As it is a treatable disease, it is of paramount importance to detect nerve impairment early in the disease as it can help in the prevention of disability. Electrophysiologic examination of the peripheral nerves is a noninvasive and sensitive method in the early detection of neuropathy. Nerve conduction study can detect the functional derangement of nerves prior to the clinical manifestations of symptoms and signs. Reduction of NCV and worsening of EMG indicate failure of medical treatment and are an indication for surgical intervention. Radiologic examination helps in evaluating the extent of bone involvement and the risks of a pathological fracture in a patient of leprosy. High-resolution ultrasonography is a noninvasive imaging technique that provides accurate morphologic information about peripheral nerves using the improvised spatial and contrast resolution. Vital information on nerve structure, morphology, vascularity, and real-time blood flow in the nerve contributes to the diagnosis and assessment of nerve damage in leprosy. MRI is a sensitive modality which helps in detecting early neuro-arthropathic changes and soft tissue changes.

Keywords Neuropathy · Nerve conduction study · High-resolution ultrasonography

Introduction

Leprosy is a chronic infectious granulomatous disease caused by *Mycobacterium leprae* which involves the skin and peripheral nerves [1]. Among peripheral nerve disorders, leprosy is a common treatable disease. Early detection of nerve impairment is very important in the management of leprosy as it can help in the prevention

M. Pinto · M. Manjunath Shenoy (✉)
Department of Dermatology, Venereology & Leprosy, Yenepoya Medical College, Mangalore, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_4

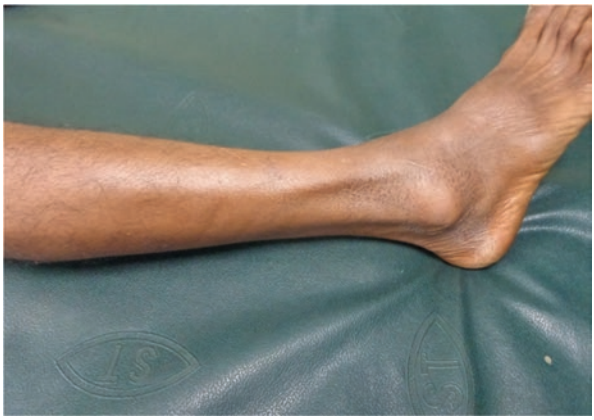

Fig. 4.1 Visibly thickened superficial peroneal nerve

of disability. Very often, there may be a visible (Fig. 4.1) or palpable grossly thickened peripheral nerve with clinical examination itself which is sufficient to analyze the neurological defects. Early nerve involvement often necessitates electrophysiological and imaging studies. Bone and vascular changes are identified only by the imaging workup. This chapter highlights the utility of noninvasive investigations like electrophysiological studies and radiological investigations in the comprehensive management of leprosy.

Electrophysiological Studies

Electrophysiologic examination of the peripheral nerves is a sensitive method in early detection of neuropathy when compared with quantitative thermal sensory, vibrometry, dynamometry, monofilament testing, and voluntary muscle testing. These studies have become useful diagnostic tools in the assessment of nerve function in leprosy. They provide vital information to confirm or alter a clinical diagnosis and can prevent major diagnostic errors.

Nerve Conduction Study (NCS)

Direct involvement of the peripheral nerve is the most important outcome of leprosy. The varied manifestations of nerve damage in leprosy include silent neuropathy, loss of tactile sensations, dryness, muscle weakness, atrophy, or contracture.

NCS involves the recording, display, measurement, and interpretation of action potentials arising from the peripheral nerves. It can detect the functional derangement of nerves before the appearance of clinical signs and symptoms [2]. Detection and early treatment of nerve function impairment (NFI) can reduce disability and deformity. Trained technicians are able to perform these tests at a faster pace with the availability of modern, affordable, and portable electrophysiology machines [3].

Principles

NCS involves application of a depolarizing square wave electrical pulse to the skin over a peripheral nerve, producing (1) a propagated nerve action potential recorded at a distant point over the same nerve and (2) a compound muscle action potential (CMAP) arising from activation of muscle fibers in a target muscle supplied by the nerve [4].

The two methods to stimulate a nerve include skin surface stimulator or a needle placed close to a nerve or a nerve root. Motor studies are performed by electrical stimulation of a nerve and recording the CMAP from surface electrodes overlying a muscle supplied by that nerve [5].

Interpretation

The interpretation of electrophysiological functions of nerve trunks is carried out using distal latency (myelination), amplitude (number of axons), and velocity (myelination).

Latency is the time from stimulus artifact to the onset of the response. In motor nerve studies, this latency includes nerve conduction time and neuromuscular transmission time. Proximal latency starts at the proximal stimulation point and ends at the first deflection from baseline. Distal latency is measured from the distal stimulation point to the first deflection from the baseline.

Amplitude is dependent on the number of axons that conduct impulses from the stimulus point to the muscle, number of functioning motor endplates, and muscle volume. The amplitude is measured from the baseline to the negative peak.

Conduction velocity (CV) is calculated by dividing the length of the nerve segment between the two stimulation points by the difference between the proximal and distal latency [6].

In sensory conduction studies, sensory nerve action potential (SNAP) is obtained by electrically stimulating sensory fibers by using supramaximal stimulus and recording the nerve action potential at a point further along that nerve.

NCS and Leprosy

NCS can detect subclinical leprosy neuropathy, which is helpful for prevention of clinical neuropathies [7].Slowing of sensory velocity and motor nerve conduction velocity (NCV) is observed in patients without any clinical abnormality which represent the preclinical stage of damage. Ramadan et al. in their study found significant reduction in MNCV, prolongation of distal latency, and reduction of amplitude [8]. Amplitude has been found to be the most affected parameter, followed by velocity and latencies by Sunki K et al. in their study [9]. Early involvement of sensory nerves with marked amplitude changes in motor nerves has been reported in leprosy [10].

Electromyography (EMG)

Principles

Electromyography (EMG) studies the electrophysiological activity of resting and contracting skeletal muscle. Detection and recording of the electrical activity from a portion of a muscle by recording of motor unit potentials are accomplished by EMG. The usual method employed followed in the study of leprosy patients is needle EMG.

Muscles selected for the EMG studies should be superficial, easily identified, and should be located away from major vessels and nerve trunks. Abductor pollicis brevis is used for testing the function of the median nerve, abductor digiti minimi for testing the ulnar nerve, and extensor digitorum brevis for testing the lateral popliteal nerve [8]. EMG is performed separately for each muscle to be tested.

Interpretation

The abnormal EMG findings indicating neuropathy include fibrillation, fasciculation, giant motor unit potentials, and incomplete interference or reduced recruitment pattern. DeFaria CR et al. have documented that motor and sensory amplitude reduction was the earliest and the most frequent encountered abnormality among their patients [11].

EMG and Leprosy

Applications of EPS in leprosy [12].

1. Early detection of subclinical neuropathy.
2. Management of neuritis.

   Based on EMG and NCV, several guidelines have been listed for indications of surgery in leprosy [13].

   - Recent neuritis: Reduction of NCV and worsening of EMG indicate failure of medical treatment and are an indication for surgical intervention.

   Stable NCV/EMG with a clinical background of subclinical neuritis warrants continuation of pharmacotherapy.

   - Long-standing neuritis: Surgery is contraindicated in a patient of leprosy with clinically complete sensory-motor deficits, and EMG/NCV results are abnormal.

3. Monitoring the Medical Treatment
   - NCV of a patient shows improvement with treatment.
   - Drug efficacy in leprosy reactions can be monitored using MNCV.
4. Detection of Thalidomide-Induced Peripheral Neuropathy: Features of Thalidomide-Induced Neuropathy Include Reduction in SNAP Amplitude and Relative Conservation of NCV [14]

The limitation of EPS is that it does not always allow assessment of the exact location, cause, and extent of a nerve lesion and coexistent disease of surrounding tissues.

Radiologic Examination

Leprosy can involve the bones and soft tissue due to direct invasion or by indirect influence due to neuropathy. It can be detected by ordering suitable radiological interventions. Radiological investigations relevant in leprosy include the conventional radiography of the hands, feet, and face, high-resolution ultrasonography (HRUS), and magnetic resonance imaging (MRI). Objectives of the radiological assessment of leprosy in principle include the conventional radiography for the bone changes, HRUS for the structural nerve changes, and MRI for the soft tissue and neuro-arthropathic changes.

Radiography of the Hands, Feet, and Face

Preliminary radiographs are necessary in assessing the extent of bone involvement and the risks of a pathological fracture in a patient of leprosy. Their utility has been explored more frequently in recent times after the advent of higher-resolution imaging techniques. They are useful in the assessment of the structural changes which generally cannot be assessed by clinical examination.

Hands and Feet

The hands and feet are commonly affected by leprosy especially in lepromatous leprosy and type 1 lepra reaction. Radiological examination (antero-posterior (AP), lateral or oblique skiagrams) of both the hands and feet is necessary to look for the presence of the bone changes, heel infections, and suspected tarsal infections.

Nonspecific changes include bone erosions, absent phalanges (resorption of digits), osteomyelitis (atrophy or trauma), tarsal disintegration, and disuse osteoporotic changes.

Specific changes due to direct infiltration by *M. leprae* can present with bone cysts or pseudocysts and sequestrate, honeycomb appearance, enlarged nutrient foramina, subarticular erosions, concentric cortical erosions (pencilling or sucked candy appearance), and osteoporosis with lepromatous arthritis [15, 16]. Patients of lepra reactions may show terminal tuft dissolution (juxta-articular decalcification), destruction/erosion of epiphyseal bone, sclerosis, subperiosteal bone erosion, and osteoperiostitis [17].

Face

Atrophy of anterior nasal spine and maxillary alveolar process are the features to look for on radiologic evaluation [18]. Paranasal sinuses are an important reservoir of *M. leprae* in MB leprosy. CT scan of paranasal sinus studies can reveal localized or diffuse thickening of mucosa and opacity of the sinus [19]. Ethmoid sinuses are most frequently affected, followed by maxillary sinus, while frontal and sphenoid sinuses are least affected. The findings of the study by Kiris A et al. suggest that persistent infection is common among lepromatous leprosy patients, despite previous treatment [20]. Hence, paranasal sinus CT examination is a useful method of evaluating patient response to treatment and follow-up.

High-Resolution Ultrasonography (HRUS)

Principles

HRUS is a noninvasive, cost-effective imaging technique that enables real-time examination of soft tissues in static and dynamic states. It gives significant information on nerve structure, morphology, and vascularity in the nerve, and this adds a new dimension in diagnosing leprosy particularly pure neuritic type and assessment of nerve damage which can prevent disabilities.

Clinical examination of nerves in leprosy is subjective and can be inaccurate. Hence, HRUS can delineate peripheral nerves in the upper and lower with accurate morphologic information using the improvised spatial and contrast resolution. It also helps in the evaluation of both entrapment and peripheral neuropathy.

HRUS with a broadband frequency ranging from 10 to 14 MHz, color Doppler (CD) with broadband frequency of 6–18 MHz, and linear array transducer are utilized for the imaging of peripheral nerves. Settings of color Doppler ultrasound

examination are set to detect signals from low flow velocity vessels in the nerves. After B-mode imaging of the nerve, a color box is put over a small part of the nerve in its longitudinal axis. Sequential increase in color gain till color bleed (noise) appears in the color box is performed, and the color gain is kept just lower to this to avoid the noise. The frequency of pulse repetition is set to pick up very low blood flow with avoidance of noise in the image and arterial pulsations. No significant arterial pulsations are detected in normal nerves. The detection of blood flow signals in the perineural plexus or intrafascicular vessels during imaging is taken as a sign of nerve hypervascularity.

Parameters Assessed

1. Cross-sectional area (CSA): It is determined from the area within the inner margin of the hyperechoic rim. This helps in assessing peripheral nerve enlargement (Fig. 4.2) [21].
2. Echogenicity: The echo density of the nerves assessed on imaging can be graded as follows: mild, some hypoechogenicity; moderate, obvious hypoechogenicity; and severe, absence of any fascicular pattern. Nerves were classified as abnormal if they showed hypoechoic or hyperechoic areas or focal thickening with loss of the normal fascicular pattern.
3. Size of fascicles: Enlarged fascicles have been reported in patients with leprosy [22].

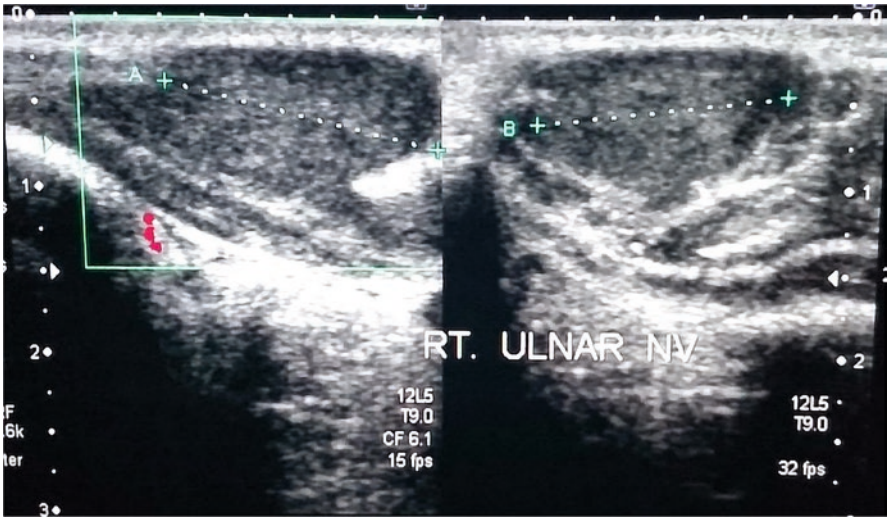

Fig. 4.2 High-resolution ultrasonography showing enlarged size and hyperechoic structures within indicative of a thickened right ulnar nerve

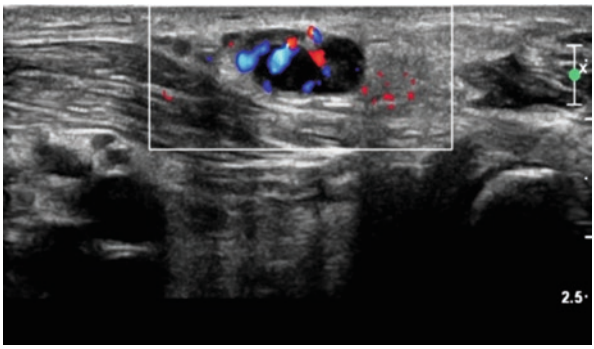

Fig. 4.3 High-resolution ultrasonography with Doppler displaying increased vascularity of a hypoechoic peripheral nerve

4. Thickness of the epineurium: HRUS has shown that the epineurium of the ulnar nerve is often strikingly thickened in leprosy patients when involved [23].
5. Vascularization of a peripheral nerve: Increased neural vascularity (Fig. 4.3) with interfascicular edema reflects immune-mediated inflammation in leprosy reactions.

Interpretation

(a) Objective measurement of nerve damage by demonstrating the nerve thickening, altered echotexture, and abnormal vascularity.
(b) Detection of more extensive changes than those diagnosed clinically in nerves with clinical features of impairment of function.
(c) Calculation of the cross-sectional areas of peripheral nerves. HRUS measurement of increased nerve size is a sensitive indicator of the presence of neuropathy in leprosy [24].
(d) Study of the structural changes in nerves that cannot be biopsied especially the mixed nerves due to risk of muscle palsy.
(e) HRUS can examine the nerve for a longer length when compared with MRI which can evaluate only a defined segment [25].

Since ultrasonography is an operator-dependent imaging modality, it requires a high level of expertise. It also requires higher-resolution ultrasound machines with color Doppler settings to assess the nerve diameter and vascularity changes.

Magnetic Resonance Imaging

Principles

MRI is an operator-independent imaging modality. MRI can distinctly delineate a nerve from surrounding soft tissues, precisely visualize nerve fascicles, and clearly localize the site of the pathology. In leprosy, peripheral nerve involvement ranges

from nerve thickening with preserved fascicular architecture to disruption of fascicular architecture and formation of micro-abscesses. Large abscesses are formed by coalescence of micro-abscesses which extend into the surrounding soft tissue [25].

Interpretation

MRI findings in leprosy are nonspecific and may show diffuse edema and swelling of the involved nerve. Findings of nodules or nerve sheath granulomas are suggestive of leprosy. Nerve abscesses appear hypointense on T1-weighted images and hyperintense on T2-wighted images and show peripheral enhancement on postcontrast study [26].

MRI is a sensitive modality in ascertaining early neuro-arthropathic changes such as degradation and interruption of the subcutaneous fat and effusion and synovitis of the metatarsophalangeal joints in leprosy patients [27]. MRI is more accurate in detecting soft tissue changes, such as subcutaneous fat infiltration, cellulitis, and abscess [28].

Conclusion

Electrophysiological and radiological investigations are the noninvasive tools that aid in the clinical findings of leprosy. They are useful objective tools in assessing the structural and functional impairments which may alter the course of treatment in leprosy. It could be stated that electrophysiological studies help in demonstrating and detecting the integrity of nerve function in leprosy. They are useful not only in assessing nerve function at the time of diagnosis but also during the follow-up of leprosy patients as a supplement to clinical tests for nerve function assessment. Radiological assessment is recommended in cases of leprosy that clinically predicts early bone changes. HRUS is a noninvasive, cost-effective tool that gives significant information on nerve structure, morphology, vascularity, and real-time blood flow in the nerve, and this information adds a new dimension to the diagnosis of leprosy and assessment of nerve damage which can prevent disabilities. Routine use of HRUS improves the diagnosis of leprosy and assesses extent and severity of nerve involvement. MRI, though not commonly used, is a sensitive tool in assessing the soft tissue changes and early neuroarthropathy. The electrophysiological and radiological studies will help the clinicians to understand the gravity of the damage caused by leprosy and timely institution of therapeutic and preventive interventions. Objective of leprosy treatment is the prevention of permanent loss of function, deformities, and disabilities.

Acknowledgments Dr. Swetalina Pradhan for USG image.
Dr. Ashwini Babu for the clinical and ultrasonographic images.

References

1. Jopling WH, Mcdougall AC. The disease. In: Hand book of leprosy. 5th ed. New Delhi: CBS Publishers and Distributors; 1996. p. 10–53.
2. Ooi WW, Srinivasan J. Leprosy and the peripheral nerve system: basic and clinical aspects. Muscle Nerve. 2004;30:393–409.
3. Vasanthy B, Chandrathil VP, Haris AA, George J. Nerve conduction study for early detection of leprosy. Int J Med Health Res. 2018;4:4–8.
4. Indu Krishnan MU, Sobhanakumari K, Jose P, Amitha NP, Irimpan KJ. High resolution ultrasound, nerve conduction study, and other non-invasive investigations in leprosy. J Skin Sex Transm Dis. 2021;3(2):136–42. https://doi.org/10.25259/JSSTD_1_2021.
5. Mallik A, Weir AL. Nerve conduction studies: essentials and pitfalls in practice. J Neurol Neurosurg Psychiatry. 2005;76:ii23–31.
6. Vashisht D, Das AL, Vaishampayan SS, Vashisht S, Joshi R. Nerve conduction studies in early tuberculoid leprosy. Indian Dermatol Online J. 2014;5(Suppl S2):71–5.
7. Marahatta S, Bhattarai S, Paudel BH. Electrophysiological profiles of leprosy neuropathy. Lepr Rev. 2017;88:373–80.
8. Ramadan W, Mourad B, Fadel W, Ghoraba E. Clinical, electrophysiological, and immunopathological study of peripheral nerves in Hansen's disease. Lepr Rev. 2001;72(1):35–49.
9. Sunki K, Koneti BB, Sreerangapuri N, Mounika Y, Pinjala P, Prasad JV. Nerve conduction study: can it diagnose leprosy early? Int J Res Dermatol. 2020;6:161–6.
10. Samant G, Shetty VP, Uplekar MW, Antia NH. Clinical and electrophysiological evaluation of nerve function impairment, following cessation of multidrug therapy in leprosy. Lepr Rev. 1999;70:10–20.
11. DeFaria CR, Silva IM. Electromyographic diagnosis of leprosy. Arq Neuropsiquiatr. 1990;48(4):403–13.
12. Gupta P, Mainra A, Dhanta A. Nerve conduction studies in leprosy a review. IOSR J Dent Med Sci. 2018;17:27–32.
13. Carayon A, Rigal J. Value of electrophysiological investigation for therapeutic indications in leprous neuritis. Med Trop(Mars). 1972;32:9–21.
14. Sheskin J, Magora A, Sagher F. Motor conduction velocity studies in patients with leprosy reaction treated with thalidomide and other drugs. Int J Lepr. 1969;37:359–64.
15. Thappa DM, Sharma VK, Kaur S, Suri S. Radiological changes in hands and feet in disabled leprosy patients: a clinicoradiological correlation. Indian J Lepr. 1992;64:58–66.
16. Ankad BS, Hombal A, Rao S, Naidu VM. Radiological changes in the hands and feet of leprosy patients with deformities. J Clin Diagn Res. 2011;5:703–7.
17. Mohammad W, Malhotra SK, Garg PK. Clinicoradiological correlation of bone changes in leprosy patients presenting with disabilities/deformities. Indian J Lepr. 2016;88:83–95.
18. Christensen VM, Bakke SN, Melson RS, Waaler E. Changes in the anterior nasal spine of the alveolar process of the maxillary bone in leprosy. Int J Lepr. 1952;20:335–40.
19. Srinivasan S, Nehru VI, Bapuraj JR, Sharma VK, Mann SB. CT findings in involvement of the paranasal sinuses by lepromatous leprosy. Br J Radiol. 1999;72:271–3.
20. Kiris A, Karlidag T, Kocakoc E, Bozgeyik Z, Sarsilmaz M. Paranasal sinus computed tomography findings in patients treated for lepromatous leprosy. J Laryngol Otol. 2007;121(1):15–8.
21. Jain S, Visser LH, Praveen TL, Rao PN, Surekha T, Ellanti R, et al. High-resolution sonography: a new technique to detect nerve damage in leprosy. PLoS Negl Trop Dis. 2009;3:e498.
22. Beekman R, Visser LH, Verhagen WI. Ultrasonography in ulnar neuropathy at the elbow: a critical review. Muscle Nerve. 2011;43(5):627–35.
23. Visser LH, Jain S, Lokesh B, Suneetha S, Subbanna J. Morphological changes of the epineurium in leprosy: a new finding detected by high-resolution sonography. Muscle Nerve. 2012;46(1):38–41.

24. Elias J, Nogueira-Barbosa MH, Feltrin LT, Furini RB, Foss NT, Marques W, et al. Role of ulnar nerve sonography in leprosy neuropathy with electrophysiologic correlation. J Ultrasound Med. 2009;28:1201–9.
25. Martinoli C, Derchi LE, Bertolotto M, Gandolfo N, Bianchi S, Fiallo P, et al. US and MR imaging of peripheral nerves in leprosy. Skelet Radiol. 2000;29:142–50.
26. Hari S, Subramanian S, Sharma R. Magnetic resonance imaging of ulnar nerve abscess in leprosy: a case report. Lepr Rev. 2007;78:155–9.
27. Luyckx G, Vanhoenacker FM, Parizel PM. Exotic pathology of the hand and foot. A pictorial review. JBR–BTR. 2008;91:160–5.
28. Maas M, Slim EJ, Heoksma AF, van der Kleij AJ, Akkerman EM, den Heeten GJ, et al. MR imaging of neuropathic feet in leprosy patients with suspected osteomyelitis. Int J Lepr Other Mycobact Dis. 2002;70(103):97.

Chapter 5
Serological and Molecular Investigations in Leprosy

Tarun Narang and Shilpa

Abstract One of the most important and crucial aspects of leprosy control and elimination has been early diagnosis and treatment. Although we have been able to eradicate leprosy as a public health issue in many countries around the globe, its prevalence or new case diagnosis rate has not decreased significantly in the endemic countries over the last 15 years. The transmission of the disease and delayed detection of cases leading to deformities and even transmission are the major deterrents in our efforts to eradicate leprosy. Clinical criteria and slit skin smear (SSS) are the commonly used diagnostic modalities for leprosy. However, SSS is not practiced in most of the places due to increased risk of HIV/HBV/HCV and lack of expertise; hence, the diagnosis is based on clinical criteria only, which may miss some cases like polar lepromatous leprosy or pure neural leprosy. Extensive research has been carried out in the past to develop different serological and molecular assays for the diagnosis of leprosy. PGL-1 and LID-1 proteins are useful in serological testing; however, they have shown poor sensitivity in detection of paucibacillary and pure neuritic leprosy. The molecular-based approaches such as polymerase chain reaction (PCR) and real-time PCR are promising techniques for the diagnosis of leprosy because of higher sensitivity and specificity, but they are not feasible for use in the field settings due to requirement of equipment, setup, and expertise. We are still far from getting a rapid, easy point-of-care test for the diagnosis of leprosy as none of these diagnostic tests described are recommended by WHO for use in diagnosis of cases and contacts. Combination of both serological and molecular techniques will improve the leprosy diagnostics and will be helpful in diagnosis as well as monitoring the response to treatment as well.

Keywords Leprosy · Real-time PCR · qPCR, ELISA · Phenolic glycolipid-1 Leprosy · IDRI protein-1

T. Narang (✉) · Shilpa
Department of Dermatology, Venereology and Leprology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_5

Introduction

Overview

Mycobacterium leprae (*M. leprae*) is the causative agent of leprosy, a chronic infectious disease with dermato-neurological and incapacitating symptoms. Despite various global initiatives to eradicate this disease, countries like India, Bangladesh, and Brazil still have high annual new case detection rates and it remains a public health issue. In this regard, WHO has designated the reduction of new cases as a priority in its global strategy, emphasising the importance of early detection, which seeks to minimise disease transmission in the population by early diagnosis of the suspicious case and contacts [1]. It is thought that a large number of people might have subclinical infection which self-heals with only minor symptoms. However, if untreated, leprosy may lead to a stage where it causes permanent nerve damage, including severe sensory and motor nerve loss, deformity, and blindness. It is already confirmed that sooner a leprosy patient is diagnosed and treated, the higher their chances of recovery. Identifying leprosy patients based on antigen-specific responses, ideally before the onset of symptoms, may seem to have a significant impact on clinical outcome [2].

Clinical criteria and slit skin smear (SSS) are the commonly used diagnostic modalities for leprosy. However, SSS is not being done in most of the places and in the field; hence, the diagnosis is based on clinical criteria only, which may miss some cases like polar lepromatous leprosy, histoid leprosy, and pure neural leprosy [3].

Early diagnosis and treatment have been the central tenets of leprosy control programmes. Early diagnosis is defined as diagnosis and start of treatment before onset of nerve impairment. Diagnosis of *M. leprae* at initial stages and early start of its treatment is essential not only for cure and prevention of deformities, but it may also prove useful in checking the transmission by earlier detection of multibacillary cases, but we need better diagnostic tests which could help in detecting leprosy cases that are missed by the clinical examination and slit skin smear examination.

Diagnosis of Leprosy

The detection of leprosy depends on existence of at least one of the three cardinal signs which include presence of skin lesions (that can vary widely in colour, appearance, and form) and existence of thickened or swollen peripheral nerves accompanied with varying degree of sensory loss, muscle weakness, and presence of acid-fast bacilli in the skin [4].

Detection of AFB in scraping of the skin is one of the cardinal signs for diagnosis of leprosy, and slit skin smear (SSS) has been one of the standard and most commonly used techniques, which has been discontinued over the last few years. It

needs to be reintroduced in the leprosy control programmes as it is not only helpful in early diagnosis of multibacillary cases of leprosy, but it also helps in assessing the response to treatment and stratification of cases as far as the risk of reactions and deformities is concerned.

Slit skin smears and histopathology of the skin are useful diagnostic modalities, but they also have their limitation for diagnosis as well as large-scale implementation in the leprosy control programmes. There is an urgent need for diagnostics (tests) that are inexpensive, specific, user-friendly, fast, accurate, and simple to deliver to end users. Broad surveys to determine the prevalence of leprosy in a given region would also benefit from such studies. Over the last few years, there has been a lot of research on the genomic structure and immune-pathogenesis of leprosy, and this has led to discovery of some useful antigens and techniques which are helpful in the diagnosis of leprosy.

The diagnostic tests used in leprosy can be broadly classified as bacterial tests which identify the bacillus in the samples like the SSS or the molecular tests like PCR or RT-PCR and the immunological tests which pick up the tissue or the immune response to the bacilli like serological tests against various leprosy antigens (PGL-1, LID-1).

Serological Investigations

Different mycobacterial antigens have been studied for the serological assays, and the basic principle is to study the antibodies directed against the antigen by using techniques like ELISA, agglutination, and lateral flow tests. Immunochromatographic lateral flow assay, detecting IgM antibodies against PGL-I and IgG antibodies to LID-1, is being developed as a point-of-care test for diagnosis of leprosy. We will be discussing some of the antigens which have been studied and have shown promise to be used for the diagnosis of leprosy (Table 5.1).

Phenolic Glycolipid-1 (PGL-1)

Phenolic glycolipid-1 (PGL-1) is an immunodominant antigen which induces a strong humoral immune response, mainly immunoglobulin M (IgM) which is measured using ELISA [5]. Brennan and Barrow in 1980 discovered PGL-1, and it was used by Payne et al. for the first time in serological studies in 1982. Identification of anti-PGL-1 antibody through ELISA is directly proportional to bacillary load which helps in classifying the severity of disease and also the response to treatment. During the treatment, decreased titre in anti-PGL-1 antibody is followed by antigen elimination and can correlate with BI [6]. However, PGL-1 antigen can persist in tissues for a long duration of time, even in the absence of live bacilli [7]. Therefore, positive anti PGL-1 titre is not always indicative of progressive disease [8, 9]. Although its

Table 5.1 Serological testing antigens and methods

Antigens	Presence in *M. leprae*	Efficacy	Drawbacks
Phenolic glycolipid-1	Cell wall protein of *M. leprae*	80–100% sensitivity in MB patients	1. Low titres in paucibacillary (PB) cases with sensitivity of 30–60% 2. No cut-off point for anti-PGL-1 titre to differentiate between disease and subclinical infection in leprosy patients and healthy individuals
35kD protein	Major membrane components of leprosy bacillus	98.5% sensitivity in MB patients	1. Only 46.7% sensitivity for PB patients 2. Poor performance with antibody levels near the cut-off value
LID 1 and NDO-LID	Protein	83.3% and 87%, respectively, sensitivity in MB patients	15.4% and 21.2%, respectively, in PB cases
IFN-γ	Pro-inflammatory marker against *M. leprae*	*M. Leprae* protein in combination with interferon gamma release assay (IGRA) provides better diagnosis	It can be detected in population who have developed sufficient immunity against *M. leprae*

performance in PB and pure neural leprosy cases is limited, serum anti-PGL-1 antibody response is a relatively reliable and simple method which is helpful to confirm diagnosis of MB leprosy and has even been used for prediction of type 2 lepra reactions [10–12].

35kD Protein

The epitope on the 35kD antigen of *M. leprae* reacts directly with MLO3-A1 monoclonal antibody [13]. Recent studies revealed that MLO3 shares 82% of its DNA and 90% of its amino acids with *M. avium also*, another species of mycobacterium [14]. Another specific sequence for 35kD, MLO4, is also used for serological tests. Initially developed as a radioimmunoassay based on competitive inhibition between patient's serum and I-125-labelled MLO4 [15], this assay eventually standardised as an ELISA using MLO4-labelled horse radish peroxidase [16, 17]. Despite the fact that this 35kD antigen shares certain genes with *M. avium*, *M. kansasii*, and *M. paratuberculosis*, the standardised serodiagnostic assay for leprosy diagnosis was found to be 97.5% precise and 90% sensitive [18]. Later, purified recombinant 35kD (r35kDa) protein was used and found 94.3% specific. The sensitivity for MB and PB cases was 83% and 17%, respectively. The presence of cross-reactive mycobacterial proteins of *M. smegmatis* in the cloned purified recombinant protein or the presence

of subclinical infection in the exposed contacts could explain the low sensitivity of the r35kD antigen assay [19].

M. Leprae *Recombinant Proteins and Development of LID-1 and NDO-LID Rapid Test*

The sequencing of *M. leprae* genome provided the opportunity for generation of protein diagnostic candidates, and a new fusion protein was developed by the Infectious Disease Research Institute, Seattle, USA, i.e., leprosy IDRI protein-1 (LID 1), which has expression of ML0405 and ML2331 antigens that have shown good immunogenicity in the serological assays and were considered appropriate alternatives for rapid diagnosis [20]. LID 1 can also be used as a carrier protein for the NDO to yield NDO-LID. Anti-natural octyl disaccharide-leprosy IDRI diagnostic (NDO-LID) is a ready-to-use kit for testing in the field and gives results within 20 min of charging of samples. Using this NDO-LID rapid diagnosis, the sensitivity and accuracy in detecting MB cases were found to be 87% and 96.1% [21].

IgA Antibody-Based Test

Salivary samples are used for the diagnosis of *M. leprae* using *M. leprae*-specific IgA antibodies in order to overcome the problem of invasive sampling. Different studies have used assays to measure salivary IgA/IgM antibodies against PGL-1 in patients and contacts and have found good correlation with serum IgM levels and recommend its use as a diagnostic tool for the contacts of leprosy patients [22]. Major problem with the serological assays in diagnosis of leprosy is their poor performance for detection of paucibacillary and pure neuritic leprosy.

Cytokines/Chemokines as Biomarker in Leprosy

During *M. leprae* infection, T cells get activated and secrete IFN-γ(interferon gamma) which is a pro-inflammatory marker against *M. leprae* and *M. tuberculosis* [23]. IFN-γ can be used as a marker for the diagnosis of *M. leprae*; however, we cannot differentiate between patients who have the disease and those who only have the infection or people who have been treated.

Moreover, immunopathogenicity induced by *M. leprae* infection activates host immune cells which secrete various effector and regulatory molecules. IL-1β, MIP-1, and MCP-1 can be used to differentiate pathogenic immunological responses existing in mycobacterial disease patients from those induced through asymptomatic *M. leprae* exposure.

Lastly, *M. leprae* protein such as ML-2478 in combination with interferon gamma release assay (IGRA) can be used as a novel method for anticipating the extent of *M. leprae* transmission in a given population and identifying people who are prone to contracting *M. leprae* infection and acquiring leprosy [24].

Gene-Based Assays

Molecular approaches like polymerase chain reaction (PCR) or real-time (RT)-PCR are routinely used for identification of specific *M. leprae* DNA sequence in clinical samples. These are highly sensitive assays which can be used for diagnosis of infection in doubtful/difficult cases, for assessing bacterial load, for detection of drug resistance, and for monitoring the response of treatment.

M. Leprae-*Specific PCR*

M. leprae-specific PCR could be carried out on routine basis in laboratory using DNA isolated from a wide range of biological specimens such as blood, skin smear, saliva, skin biopsy, oral or nasal swab, nerve section, and urine [25–28]. Detection range of *M. leprae* using PCR ranges between 10 and 30 fg which is equivalent to 2.8–8.3 bacilli [29]. Few *M. leprae*-specific PCR genes are RLEP, hsp85, 18 kDa, 36 kDa, 16S rRNA, and sodA (Table 5.2). Among these, the most sensitive and specific gene target-based PCR is *M. leprae*-specific repetitive element (RLEP) PCR [30]. The sensitivity of PCR is 100% in patients with a positive bacteriological index and lower in case of patients having low or negative bacteriological index.

Table 5.2 Comparative analysis of immunological and molecular markers in diagnosis of leprosy

Assay	Multibacillary patient's positivity (%)	Paucibacillary patient's positivity (%)
PGL-1 ELISA	80–100	30–60
35kD ELISA	98.5	46.7
r35kD ELISA	83	17
NDO-LID rapid test	87	21.2
PCR-using gene target RLEP	100	73
PCR-using 16S rRNA gene target	100	50
PCR-using 18 kDa gene target	99	74
PCR-using proline-rich antigen, 36 kDa	87–100	36–60

Multiplex PCR (M-PCR)

M-PCR is a better alternative and sensitive type of PCR technique in which two or more set of primers are used simultaneously for amplification of different target genes present in the same reaction (Table 5.3). However, selection of primers should be done carefully on the basis of these three parameters:

(a) The primers should have similar annealing temperature.
(b) The primers should not be complementary to each other.
(c) The size of the amplicon from each primer pair must be different so that they can be easily visualised as distinct bands by gel electrophoresis.

In *M. leprae* clinical diagnosis, M-PCR employs more than one specific gene to its DNA. This technique is used for the detection of paucibacillary forms or indeterminate leprosy by targeting pseudo genes of *M. leprae* such as ML1545, ML2180, and ML2179 with the positive detection range of 75.61% [31]. In case of PB patients, the positivity rate of M-PCR has been increased from 22.2% (conventional PCR) to 80.3% [32]. Different types of clinical samples can be used like blood, nasal swab, saliva, and SSS for the detection of PB and MB cases with the help of M-PCR using RLEP, 16S rRNA, and sodA targets [33] (Table 5.4).

After amplification of individual genes, products are electrophoresed using 2% agarose gel, whereas M-PCR-amplified gene products are electrophoresed using 4% agarose gel. The products are viewed using a gel documentation system. M-PCR using multiple gene targets improves the identification of *M. leprae* DNA with respect to sensitivity and specificity.

In Silico Molecular Techniques

In silico molecular techniques for drug resistance are used for the patients who are not responding to MDT. Resistance to anti-leprosy medicines like dapsone, rifampicin, and fluoroquinolones has been detected using molecular-based techniques to find mutation in drug resistance-determining regions (DRDR). Rifampicin resistance is associated with mutation in rpoB gene sequencing coding β-subunit of

Table 5.3 Sequences for commonly used primers in PCR

Gene	Sequence	Primer orientation	Amplicon size
16S rRNA	Forward	5′-CGGAAAGGTCTCTAAAAAATCTT-3′	171 bp
16S rRNA	Reverse	5′-CATCCTGCACCGCAAAAAGCTT-3′	
sodA	Forward	5′-CAGCTGTATGACCAACAGGC-3′	185 bp
sodA	Reverse	5′-TGCGTCTTAGATGTTGCAGC-3′	
RLEP	Forward	5′-TGCATGTCATGGCCTTGAGG-3′	129 bp
RLEP	Reverse	5′-CACCGATACCAGCGGCAGAA-3′	

Table 5.4 Sensitivity and specificity of different primers and different samples for diagnosis of leprosy

Clinical sample.	Target											
	M-PCR			RLEP			16S rRNA			sodA		
	Positivity(%)	Sensitivity	Specificity	Positivity (%)	Sensitivity	Specificity	Positivity (%)	Sensitivity	Specificity	Positivity (%)	Sensitivity	Specificity
SSS	93.33	0.93	1	51.66	0.51	1	31.66	0.31	1	21.66	0.21	1
Blood	86.66	0.86	1	46.66	0.46	1	53.33	0.53	1	53.33	0.53	1
Nasal swab	80	0.8	0.6	70	0.7	0.9	76.66	0.76	0.96	10	0.1	1
Saliva	54.48	0.548	1	45.16	0.45	1	35.48	0.35	1	6	0.06	1

RNA polymerase, dapsone resistance is associated with mutation within the folP1 sequence coding the dihydropteroate synthase (DDS), and ofloxacin resistance is associated with mutation within the gyrA sequence coding the subunit A of DNA gyrase [34]. To perform PCR for drug resistance, skin biopsy or SSS from the patient is preserved in 70% ethanol and sent to the laboratory to check mutation by gene sequencing in respective DRDR.

Loop-Mediated Isothermal Amplification (LAMP) Assay

It is a DNA amplification method that has been used to develop assays for various diseases like tuberculosis, nontuberculous mycobacteria, and COVID-19. Notomi et al. first devised this novel isothermal amplification method to amplify a limited amount of DNA copies into a million copies within an hour [35]. It utilises a set of four (or six) different primers which bind to six (or eight) different regions on the target gene making it highly specific. The end result or a positive test can be assessed easily by observing a change in turbidity or colour of the reaction with the naked eye or by using a turbidimeter or colorimeter or even a smartphone-based application for reading the colour or turbidity. It is an ideal assay for resource-constrained facilities due to minimal hardware requirements. The results can be read within an hour from the sample and the visualisation of the results is by seeing the change in colour of the analyte. Different primers have been used for the diagnosis of leprosy, a recent study by Jiang et.al developed a LAMP assay targeting the *M. leprae* RLEP gene and were of the opinion that the high sensitivity and rapidity of the LAMP assay, together with its ability to readily identify the *M. leprae* subspecies through naked eye evaluation, make it an attractive tool for routine diagnostics [36].

According to a recent meta-analysis of all leprosy diagnostic tests, agglutination tests had the highest sensitivity of the three serological tests studied (ELISA, agglutination test, and lateral flow), and all had comparable specificity. Among molecular analysis, qPCR had better sensitivity but lower specificity than traditional PCR. The PCR method was significantly more reliable than ELISA. However, the authors concluded that the findings among studies differed greatly, so they cannot suggest these tests for detection of leprosy patients due to heterogeneity in variation, thresholds, antigens targeted, and concerns about study aspect [37].

Conclusion

Early detection and management of *M. leprae* is the need of the hour if we want to check the transmission of leprosy and fulfil our dream of a leprosy-free world. We need more robust tests that can be used in the field to screen and diagnose leprosy patients and their contacts and maybe which can help us to classify the patients into paucibacillary and multibacillary so that adequate treatment can be given to those

diagnosed with leprosy. A combination of serological and molecular testing may prove to be useful and better and help to eradicate leprosy from society in order to have a *leprosy-free world*.

References

1. WHO. Ending the neglect to attain the sustainable development goals: a road map for neglected tropical diseases 2021–2030. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO
2. Kumar B, Dogra S. Leprosy: a disease with diagnostic and management challenges! Indian J Dermatol Venereol Leprol. 2009;75:111–5.
3. Martinez AN, Talhari C, Moraes MO, Talhari S. PCR-based techniques for leprosy diagnosis: from the laboratory to the clinic. PLoS Negl Trop Dis [Internet]. 2014;8(4):e2655. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3983108/.
4. Leprosy WEC on, Organization WH. WHO expert committee on leprosy: eighth report. World Health Organization; 2012. https://apps.who.int/iris/handle/10665/75151.
5. Brennan PJ, Barrow WW. Evidence for species-specific lipid antigens in mycobacterium leprae. Int J Lepr Mycobact Dis Off Organ Int Lepr Assoc. 1980;48:382–7.
6. Chin-a-Lien RA, Faber WR, van Rens MM, Leiker DL, Naafs B, Klatser PR. Follow-up of multibacillary leprosy patients using a phenolic glycolipid-I-based ELISA. Do increasing ELISA-values after discontinuation of treatment indicate relapse? Lepr Rev. 1992;63:21–7.
7. Meeker HC, Schuller-Levis G, Fusco F, Giardina-Becket MA, Sersen E, Levis WR. Sequential monitoring of leprosy patients with serum antibody levels to phenolic glycolipid-I, a synthetic analog of phenolic glycolipid-I, and mycobacterial lipoarabinomannan. Int J Lepr Mycobact Dis Off Organ Int Lepr Assoc. 1990;58:503–11.
8. Cunanan A, Chan GP, Douglas JT. Risk of development of leprosy among Culion contacts. Int J Lepr Mycobact Dis. 1998;66:S78A.
9. Fujiwara T, Hunter SW, Cho SN, Aspinall GO, Brennan PJ. Chemical synthesis and serology of disaccharides and trisaccharides of phenolic glycolipid antigens from the leprosy bacillus and preparation of a disaccharide protein conjugate for serodiagnosis of leprosy. Infect Immun. 1984;43(1):245–52.
10. Fine PE, Ponnighaus JM, Burgess P, Clarkson JA, Draper CC. Seroepidemiological studies of leprosy in northern Malawi based on an enzyme-linked immunosorbent assay using synthetic glycoconjugate antigen. Int J Lepr Mycobact Dis Off Organ Int Lepr Assoc. 1988;56(2):243–54.
11. Contin LA, Alves CJM, Fogagnolo L, Nassif PW, Barreto JA, Lauris JRP, et al. Use of the ML-flow test as a tool in classifying and treating leprosy. An Bras Dermatol. 2011;86(1):91–5.
12. Cardona-Castro N, Beltrán-Alzate JC, Manrique-Hernández R. Survey to identify mycobacterium leprae-infected household contacts of patients from prevalent regions of leprosy in Colombia. Mem Inst Oswaldo Cruz. 2008;103:332–6.
13. Mohagheghpour N, Munn MW, Gelber RH, Engleman EG. Identification of an immunostimulating protein from mycobacterium leprae. Infect Immun. 1990;58:703–10.
14. Triccas JA, Winter N, Roche PW, Gilpin A, Kendrick KE, Britton WJ. Molecular and immunological analyses of the Mycobacterium avium homolog of the immunodominant mycobacterium leprae 35-kilodalton protein. Infect Immun. 1998;66:2684–90.
15. Sinha S, Sengupta U, Ramu G, Ivanyi J. A serological test for leprosy based on competitive inhibition of monoclonal antibody binding to the MY2a determinant of mycobacterium leprae. Trans R Soc Trop Med Hyg. 1983;77:869–71.
16. Mwatha J, Moreno C, Sengupta U, Sinha S, Ivanyi J. A comparative evaluation of serological assays for lepromatous leprosy. Lepr Rev. 1988;59:195–9.

17. Sinha S, Sengupta U, Ramu G, Ivanyi J. Serological survey of leprosy and control subjects by a monoclonal antibody-based immunoassay. Int J Lepr Mycobact Dis Off Organ Int Lepr Assoc. 1985;53:33–8.
18. Triccas JA, Roche PW, Britton WJ. Specific serological diagnosis of leprosy with a recombinant mycobacterium leprae protein purified from a rapidly growing mycobacterial host. J Clin Microbiol. 1998;36(8):2363–5.
19. Roche PW, Failbus SS, Britton WJ, Cole R. Rapid method for diagnosis of leprosy by measurements of antibodies to the M. leprae 35-kDa protein: comparison with PGL-I antibodies detected by ELISA and "dipstick" methods. Int J Lepr Mycobact Dis Off Organ Int Lepr Assoc. 1999;67:279–86.
20. Duthie MS, Ireton GC, Kanaujia GV, Goto W, Liang H, Bhatia A, et al. Selection of antigens and development of prototype tests for point-of-care leprosy diagnosis. Clin Vaccine Immunol. 2008;15:1590–7.
21. Douglas JT, Cellona RV, Fajardo TT Jr, Abalos RM, Balagon MV, Klatser PR. Prospective study of serological conversion as a risk factor for development of leprosy among household contacts. ClinDiagn Lab Immunol. 2004;11:897–900.
22. Cabral PB, Júnior JE, De Macedo AC, Alves AR, Gonçalves TB, TCB C, et al. Anti-PGL1 salivary IgA/IgM, serum IgG/IgM, and nasal mycobacterium leprae DNA in individuals with household contact with leprosy. Int J Infect Dis. 2013;17(11):e1005–10.
23. Wallis RS, Pai M, Menzies D, Doherty TM, Walzl G, Perkins MD, et al. Biomarkers and diagnostics for tuberculosis: progress, needs, and translation into practice. Lancet Lond Engl. 2010;375(9729):1920–37.
24. Geluk A, Bobosha K, van der Ploeg-van Schip JJ, Spencer JS, Banu S, Martins MB, et al. New biomarkers with relevance to leprosy diagnosis applicable in areas hyperendemic for leprosy. J Immunol Baltim Md. 2012;188:4782–91.
25. Santos AR, De Miranda AB, Sarno EN, Suffys PN, Degrave WM. Use of PCR-mediated amplification of mycobacterium leprae DNA in different types of clinical samples for the diagnosis of leprosy. J Med Microbiol. 1993;39:298–304.
26. de Wit MY, Douglas JT, McFadden J, Klatser PR. Polymerase chain reaction for detection of mycobacterium leprae in nasal swab specimens. J Clin Microbiol. 1993;31:502–6.
27. Caleffi KR, Hirata RDC, Hirata MH, Caleffi ER, Siqueira VLD, Cardoso RF. Use of the polymerase chain reaction to detect mycobacterium leprae in urine. Braz J Med Biol Res. 2012;45:153–7.
28. da Rosa FB, de Souza VC, de Almeida TAP, do Nascimento VA, Vásquez FG, da GS CM, et al. Detection of mycobacterium leprae in saliva and the evaluation of oral sensitivity in patients with leprosy. Mem Inst Oswaldo Cruz. 2013;108:572–7.
29. Bang PD, Suzuki K, Phuong LT, Chu TM, Ishii N, Khang TH. Evaluation of polymerase chain reaction-based detection of mycobacterium leprae for the diagnosis of leprosy. J Dermatol. 2009;36:269–76.
30. Turankar RP, Pandey S, Lavania M, Singh I, Nigam A, Darlong J, et al. Comparative evaluation of PCR amplification of RLEP, 16S rRNA, rpoT and sod a gene targets for detection of M. leprae DNA from clinical and environmental samples. Int J Mycobacteriol. 2015;4:54–9.
31. Chaitanya VS, Cuello L, Das M, Sudharsan A, Ganesan P, Kanmani K, et al. Analysis of a novel multiplex polymerase chain reaction assay as a sensitive tool for the diagnosis of indeterminate and tuberculoid forms of leprosy. Int J Mycobacteriol. 2017;6:1–8.
32. Banerjee S, Sarkar K, Gupta S, Mahapatra PS, Gupta S, Guha S, et al. Multiplex PCR technique could be an alternative approach for early detection of leprosy among close contacts–a pilot study from India. BMC Infect Dis. 2010;10:252.
33. Pathak VK, Singh I, Turankar RP, Lavania M, Ahuja M, Singh V, et al. Utility of multiplex PCR for early diagnosis and household contact surveillance for leprosy. Diagn Microbiol Infect Dis. 2019;95:114855.
34. Cambau E, Perani E, Guillemin I, Jamet P, Ji B. Multidrug-resistance to dapsone, rifampicin, and ofloxacin in mycobacterium leprae. Lancet Lond Engl. 1997;349(9045):103–4.

35. Notomi T, Okayama H, Masubuchi H, Yonekawa T, Watanabe K, Amino N, Hase T. Loop-mediated isothermal amplification of DNA. Nucleic Acids. 2000;28:E63.
36. Jiang H, Tsang L, Wang H, Liu C. Loop-mediated isothermal amplification (LAMP) assay targeting RLEP for detection of mycobacterium leprae in leprosy patients. Int J Infect Dis. 2021;107:145–52.
37. Gurung P, Gomes CM, Vernal S, Leeflang MMG. Diagnostic accuracy of tests for leprosy: a systematic review and meta-analysis. Clin Microbiol Infect. 2019;25(11):1315–27.

Chapter 6
Treatment of Leprosy and Lepra Reactions

Santoshdev P. Rathod and Kirti Kalra

Abstract Treatment of leprosy had undergone a significant transformation from a historical regime containing chaulmoogra oil to two decades of dapsone monotherapy from the 1940s to 1960s. Discovery of sterilizing capacities of rifampicin and the need for a multidrug regimen amid rising primary dapsone resistance led to the implementation of multidrug therapy (MDT) advocated by the World Health Organization (WHO) in 1982. WHO MDT has been the most effective tool in reducing the burden of disease globally and has remained the cornerstone of leprosy therapy till now. However, apart from changes in the duration of WHO MDT regimen, there has not been much innovation. The chapter provides a broad outline of various MDT regimens, their advantages and disadvantages, and newly introduced drug regimens along with an insight into MDT regimen for leprosy in special scenarios.

Keywords Leprosy · Multidrug therapy · Paucibacillary · Multibacillary

Introduction

Leprosy, one of the oldest infectious diseases known to mankind, was first identified by Gerhard Armauer Hansen of Norway in 1873 [1]. Apart from other organs involved, it mainly affects the skin and peripheral nerves. The world has been through the rise and fall of leprosy until it reached the stage of elimination in the twentieth century. From the late nineteenth century until 1940, chaulmoogra oil extracted from *Hydnocarpus wightiana* seeds was considered the only effective way to treat leprosy [2]. Promin was the first sulfone drug used in the treatment of leprosy in 1941. Later on, Lowe and Smith, in 1949 [3], reported the successful use of oral dapsone in the treatment of leprosy, after which dapsone monotherapy became the mainstay of treatment till the 1980s.

S. P. Rathod (✉) · K. Kalra
Department of Dermatology, Smt. NHL Municipal Medical College, SCL General Hospital, Ahmedabad, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_6

Historical Regimes

Dapsone Monotherapy

GH Faget at Carville, Louisiana, was the pioneer to use dapsone for the treatment of leprosy [4]. He used promin, a derivative of dapsone via an intravenous route at a dose of 2.5 g daily [5]. Later on in 1947, dapsone itself was used for the first time by Cochrane via subcutaneous route [6]. Finally, in the 1950s, oral dapsone at a dose of 100 mg daily became the mainstay of treatment.

From 1943 until 1982, the standard treatment for lepromatous leprosy was lifelong dapsone monotherapy. Though lepromatous leprosy has the highest bacterial burden of all human diseases along with an impairment in protective cellular immunity, dapsone monotherapy proved effective despite being a bacteriostatic drug. Easy availability, cost-effectiveness, administration by oral route, and better safety profile promoted its use as monotherapy for such a long-standing period.

However, in 1964, the first case of dapsone resistance came into light due to point mutations in folP1 gene, which encodes dihydropteroate synthase [7]. Primary resistance was found in patients never put through dapsone, and secondary resistance or recurrence was identified in those previously treated with dapsone. Its use as monotherapy led to the gradual elimination of drug susceptible organisms and mutants resistant to other antimicrobials, but the dapsone-resistant mutants survived and multiplied selectively, eventually causing relapse [8].

Rifampicin Monotherapy

Rifampicin, an ansamycin, was first introduced for the treatment of leprosy in 1970 by Rees et al. [9] It targets the β-subunit of the RNA polymerase encoded by rpoB gene and blocks RNA synthesis in mycobacteria [10]. It has potent antimycobacterial activity with an ability to kill around 99% of bacilli with a single dose of 1500 mg or 3–4 daily doses of 600 mg as tested in mouse footpad [8]. This great bactericidal property due to its capability to kill intracellular bacilli along with its promising action against dapsone-resistant organisms gave it an added advantage for the treatment of this chronic infectious disease.

However, there were some challenges with the use of rifampicin, namely, its higher cost and lack of any consensus regarding the optimal dose and duration of treatment. As dapsone resistance had already become a global issue during the 1970s, similar resistance to rifampicin emerged soon due to resistance against rpoB gene [11]. These challenges were overcome when it became clear that a combination of several active drugs would be needed to maintain the efficacy of any drug regimen. The introduction of multidrug therapy (MDT) in leprosy in the 1980s was a turning point for the treatment of this stigmatized disease.

WHO MDT (WHO Multidrug Therapy)

The World Health Organization Executive Board assessed and countersigned the reports of the "Study Group on Chemotherapy of Leprosy for Control Program" on 17 May 1982, and finally the multidrug therapy came into force in 1983 [12].

MDT was introduced to address the issue of drug resistance and side effects due to prolonged use of monotherapy in addition to enhancing the effectiveness of treatment. This idea was based on the calculation that an untreated lepromatous leprosy patient carries about 11 logs of live bacilli and the proportion of the drug-resistant mutants that are expected to be occurring is estimated as 1 in 7 logs for rifampicin and 1 in 6 for dapsone and clofazimine, respectively [13]. The organisms resistant to one drug will be susceptible to the other drugs in MDT, because their mechanisms of action are different. Therefore a cocktail of several active drugs was developed as the probability of emergence of mutant resistance to any 2 drugs decreases to 1 in 13 logs, which is insignificant [13].

Since its inception in 1982, WHO MDT has undergone minor changes mainly with regard to its classification and the duration of treatment. Its evolution is highlighted in Table 6.1 [14].

Table 6.1 Evolution of MDT regimens and classification of paucibacillary and multibacillary leprosy

Year	WHO classification	WHO MDT regimens
1982 (WHO MDT)	PB: BI $< 2+$ MB: BI $\geq 2+$	PB: Rifampicin 600 mg once a month (supervised) + dapsone 100 mg daily (self-administered) for 6 months MB: Rifampicin 600 mg once a month (supervised) + dapsone 100 mg daily (self-administered) + clofazimine 300 mg once a month (supervised) and 50 mg daily (self-administered) for 2 years or till smear negativity whichever is later
1988 (WHO MDT) modified	PB: BI = 0 MB: BI $\geq 1+$	
1994 (FD-MDT 24)	PB: BI = 0 MB: BI $\geq 1+$	PB: Same as above MB: Same as above but for a fixed duration of 24 months
1998 (FD-MDT 12)	SLPB (single-lesion paucibacillary leprosy): 1 skin lesion PB: 2–5 skin lesions MB: ≥6 skin lesions	SLPB: Single supervised dose of rifampicin (600 mg), ofloxacin (400 mg), minocycline (100 mg) PB: Rifampicin 600 mg monthly plus dapsone 100 mg daily; 6 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
2003	PB: 1–5 skin lesions MB: ≥6 skin lesions	SLPB: Withdrawn PB and MB treatment regimen same as FD-MDT 12
2000 proposal	A (accompanied): MDT	Same for both PB and MB under supervision of close ones
2002 proposal	U (uniform): MDT	Uniform MDT of 6 months for both PB and MB cases

BI bacterial index, *MB* multibacillary, *PB* paucibacillary

The WHO FD-MDT Regimen [14]

PB: (1–5 skin lesions)—Rifampicin 600 mg monthly plus dapsone 100 mg daily; 6 cycles in 9 months.

MB: (≥6 skin lesions)—Rifampicin 600 mg plus clofazimine 300 mg monthly and dapsone 100 mg plus clofazimine 50 mg daily; 12 cycles in 18 months.

Image showing MDT blister packs for both paucibacillary (PB) and multibacillary (MB) leprosy in adults as well as childhood has been added in Fig. 6.1.

Fig. 6.1 **(a)** Adult MB-MDT pack. **(b)** Adult PB-MDT pack. **(c)** Child MB-MDT pack. **(d)** Child PB-MDT pack

Alternate Regimens (Non-WHO MDT)

With the advent of time, new regimens are being introduced as certain drawbacks are to be taken care of in the old multidrug therapy. A safe and effective alternative regimen is to be kept in store as emergence of drug resistance is inevitable in any large-scale treatment of a chronic infectious disease. Likewise, the transmission of disease has not been interrupted, and to break this chain of transmission, we need to cultivate new regimens. The current MDT regimen is still complicated as two types of drug administrations, i.e., monthly (supervised) and daily (self-administration), are involved. So if a patient fails to comply with self-administered daily treatment, he/she is virtually treated with rifampicin (RIF) monotherapy. Therefore, the current MB regimen is not RIF resistance-proof [15].

Thus a strong need to combat drug resistance and enhance the therapeutic efficacy has contributed to the introduction of monthly supervised regimens with new drug combinations coming into use.

Newer MDT Regimens

In recent times, certain drugs like fluoroquinolones and minocycline have been used to formulate new MDT regimens. They seem to be a good option in patients showing poor response, intolerance, or any contraindication to primary chemotherapy. Currently used newer drugs with their dose, mechanism of action, side effects, and contraindications have been enlisted in Table 6.2.

MB Cases

1. Fully supervisable, monthly administered regimens.
   - PMM combination: Rifapentine 900 mg, moxifloxacin 400 mg, and minocycline 100 mg (PMM) for 12 months [16].
   - ROM combination: Rifampicin 600 mg, ofloxacin 400 mg, and minocycline 100 mg for 12 months for MB cases.
2. 6-week quadruple regimen: Rifampicin 600 mg plus ofloxacin 400 mg plus clofazimine 100 mg plus minocycline 100 mg once a week for 6 weeks [17]
3. Once a month, supervised rifampicin 600 mg plus ofloxacin 400 mg plus minocycline 100 mg in addition to self-administered dapsone 100 mg plus clofazimine 50 mg daily for 12 months [18].

PB Cases

- Single dose of ROM or RMM for all PB cases [19].
- 4-week, ofloxacin-containing regimen: Rifampicin 600 mg and ofloxacin 400 mg given in supervised doses daily for 4 weeks
- Once a month ROM for 6 months.

Table 6.2 Currently used newer drugs in leprosy

Name of the drug and dose	Mechanism of action	Adverse effects	Contraindications
1. Rifapentine (900 mg monthly)	Inhibits DNA-dependent RNA-polymerase of the bacteria interfering with bacterial cell replication	• Nausea • Vomiting • Headache • Discoloration of body secretions	Any previous history of allergy to the drug
2. Fluoroquinolones • Ofloxacin (400 mg monthly) • Moxifloxacin (400 mg monthly)	Inhibits α subunit of DNA gyrase, interfering with bacterial DNA replication	• Nausea • Diarrhea • Headache • Insomnia • Dizziness	Relative contraindication: Pregnant women and children
3. Minocycline (100 mg monthly)	Binds reversibly to the 30 S unit of the ribosome, blocking protein synthesis	• Nausea • Diarrhea • Headache • Dizziness • Mouth sores • Discoloration of the teeth in infants or young children	Pregnancy and patients <16 years of age
4. Macrolides • Clarithromycin (500 mg OD)	Inhibits bacterial protein synthesis by binding to the 50s ribosomal subunits of bacteria	• GI upset • Dizziness • Irritability • Hallucinations • Metallic taste in the mouth and confusion	Patients with prolonged QT interval and taking class Ia and class III anti-arrhythmic agents Relative contraindication: Pregnancy

DNA deoxyribonucleic acid, *RNA* ribonucleic acid

Accompanied MDT [20]

The entire supply of MDT drugs is provided to the patient at the time of diagnosis, and someone close to or important to the patient undertakes the responsibility of helping him or her complete a full course of treatment.

Uniform MDT [21]

A fixed duration of treatment of 6 months with rifampicin, dapsone, and clofazimine as for MB therapy is given for both PB and MB cases. Relapse rate is then assessed to see the response.

The advantages and disadvantages with the mentioned regimes are summarized in Table 6.3.

Table 6.3 Advantages and disadvantages of various regimens

Regimen	Advantages	Disadvantages
WHO MDT (in current form)	1. The issue of resistance to dapsone and other drugs already in use was addressed 2. Side effects due to long-term monotherapy were overcome 3. It promoted compliance of patient due to shorter duration of treatment, thus took care of the issue of default 4. It retained rifampicin in all therapeutic regimens owing to its strong bactericidal action and good efficacy even in monthly doses 5. It is cost-effective 6. Combination of drugs like dapsone and clofazimine in daily doses along with rifampicin in supervised monthly doses works well on persisters and reduces the chances of relapse	1. Continuation of treatment, till smear negativity in MB leprosy cases is difficult from operational point of view 2. The cure or endpoint of treatment of PB cases (smear-negative patients) has been more difficult to ascertain unlike in MB cases wherein the slit skin smears indicate disease activity
WHO FD-MDT regimen	1. Better patient compliance without significantly compromising the efficacy 2. Positive BI should not be the marker of continuation of treatment as it declines gradually during follow-up and may remain positive at the end of 12 or 24 months of therapy	1. Clinical activity may not correlate well with bacteriological activity and vice versa at the end of 12 months 2. High BI (>4) denotes poor cell-mediated immunity, so the chances of relapse due to presence of dormant bacilli (persisters) are more, warranting a longer duration of treatment 3. Bacteriological relapse occurred earlier than clinical worsening, demanding a long follow-up period with slit skin smear as a part of post-therapeutic surveillance 4. Post-therapy surveillance is not recommended, and patients are advised to report as soon as they notice any clinical signs of the disease activity
Other regimens: ROM, RMM_X, PMM_X, etc.	1. The use of new drug regimens will help to avoid the emergence of drug resistance as these involve either supervised or shorter duration of treatment	1. Costlier 2. Not easily available 3. Limited evidence

(continued)

Table 6.3 (continued)

Regimen	Advantages	Disadvantages
Accompanied MDT	1. It's an easier way to give supervised therapy 2. It involves the presence of family members in sharing the burden of disease 3. Contacts can be easily identified and treated likewise	1. Lacks evidence-based justification 2. Neglects the importance of regular contacts between healthcare workers with patients 3. Delays the identification of impairment and deformity
Uniform MDT	1. Uniform MDT merges leprosy with general healthcare services making it more operationally convenient 2. Increased compliance due to shorter duration makes it an acceptable regimen for MB patients 3. Addition of clofazimine to PB regimen helps in rapid regression of granulomas and further reduces the chances of relapse	1. Overtreatment of PB leprosy patients and undertreatment of MB patients, especially those with a high initial BI, are major drawbacks of this regimen 2. Relapse rate and chances of reaction are higher in MB cases due to short duration of treatment

R rifampicin, *O* ofloxacin, *M* minocycline, *P* rifapentine, *Mx* moxifloxacin

Resistance to MDT

Resistance to multidrug therapy (MDT) is one of the major obstacles in the treatment of Hansen's disease [22]. It can manifest in two forms:

1. Primary resistance: Presence of already resistant strains.
2. Secondary resistance: Development of resistance due to inadequate therapy or monotherapy.

In cases where resistance to a standard anti-leprosy drug is identified and documented, treatment regimens may be altered for the patient.

Rifampicin-resistant MB cases: A fully supervised regimen in two phases [15] is recommended.

- The intensive phase: Moxifloxacin 400 mg—clofazimine 50 mg—clarithromycin 500 mg—minocycline 100 mg all taken daily for 6 months.
- The continuation phase: Moxifloxacin 400 mg—clarithromycin 1000 mg—minocycline 200 mg all taken once monthly for 18 months.
- If available, ofloxacin may be replaced by moxifloxacin 400 mg, which has stronger bactericidal activity against *M. leprae* [23].

It has been observed that rifampicin-resistant patients are also expected to be resistant to dapsone [24].

Defaulter

A defaulter is a person who has not completed the scheduled 6 months of PB-MDT in 9 months and 12 months of MB-MDT in 18 months. It results in subtherapeutic dosing leading to drug resistance, disease progression, and continuation of transmission. A defaulter showing signs of new skin lesions or nerve involvement and any indication of lepra reaction should be immediately put on a new course of MDT according to the classification [25]. Busting myths and misconceptions associated with the disease and a well-equipped easily approachable healthcare facility help in timely completion of treatment minimizing the possibility of default.

Relapse

Relapse indicates the reappearance of clinical leprosy in the wake of successful completion of recommended anti-leprosy treatment. It is indicated by the appearance of new skin lesions and an increase in the bacteriological index by two or more units. Several risk factors associated with relapse are presence of persisters, reinfection, inadequate/irregular therapy, drug resistance, high initial BI, number and even size of skin lesions, and negative lepromin test [26].

Treatment should be started immediately as soon as a relapsed case is identified keeping in mind certain factors like type of leprosy, prior treatment taken, and drug resistance. In fact, antibiotic resistance tests should be done before initiating any therapeutic regime. Treatment of relapse is discussed in Table 6.4 [27].

Table 6.4 Recommended treatment regimens

	Resistance	Scenario	Treatment
1.	Relapse due to persisters	Relapse after a course of MB-MDT	Retreatment with WHO MDT depending on the type of disease (PB or MB-MDT)
2.	Relapse due to dapsone resistance	Relapse after previous cure with dapsone monotherapy	Standard WHO MDT
3.	Relapse due to rifampicin resistance or dapsone and rifampicin-resistant *M. lepra*	Primary or secondary dapsone-resistant MB cases who received standard WHO MB-MDT but did not take their clofazimine (situation equivalent to rifampicin monotherapy)	Clofazimine 50 mg daily for 24 months plus two of the following drugs for 6 months: Ofloxacin 400 mg daily/ minocycline 100 mg daily/ clarithromycin 500 mg daily, followed by: Ofloxacin 400 mg daily or minocycline 100 mg daily for the remaining 18 months

MB multibacillary, *PB* paucibacillary

Treatment of Lepra Reaction

Treatment of both type 1 (reversal reaction) and type 2 lepra reaction (erythema nodosum leprosum) is imperative, as they are accountable for permanent nerve damage, deformity, and disability associated with leprosy. Multidrug therapy is continued along with specific treatment for reactions which mainly depend on its severity.

For mild type 1 reactions characterized by inflammation in few of the existing skin lesions, nonsteroidal anti-inflammatory drug (NSAID) like aspirin 600 mg every 4–6 h with meals till sign and symptoms subside is sufficient. However, supportive care with rest and splinting the affected nerve carries great value in all lepra reactions. For severe reactions showing signs of markedly inflamed skin lesions with facial involvement, ulceration, neuritis, and impending or recent paralysis, prompt treatment with oral corticosteroids and NSAIDS is mandatory. Prednisolone started at a dose of 1 mg/kg/day is continued till clinical improvement is seen followed by gradual tapering by 10 mg every fortnightly and 5 mg every 15 days from 20 mg onwards.

Type 2 lepra reaction is characterized by crops of tender, evanescent, erythematous, subcutaneous nodules associated with fever and malaise. Mild type 2 reactions showing few ENL lesions can be managed with nonsteroidal anti-inflammatory drugs for a few weeks with slow tapering as clinical improvement is seen. For severe type 2 reactions, oral corticosteroids should be started at a dose of 1 mg/kg/day till clinical improvement is seen followed by tapering every week by 5–10 mg over 6–8 weeks. For severe recurrent ENL reactions and patients showing adverse reaction to prolonged corticosteroid therapy, drugs like clofazimine at a dose of 300 mg daily for 1 month with gradual tapering by 100 mg at an interval of 3 months and thalidomide 400 mg daily for 7 days with slow reduction by 100 mg on monthly basis can be added. Alternative drugs like cyclosporine, azathioprine, pentoxifylline, mycophenolate mofetil, and betamethasone pulse therapy have also been used with variable success.

Childhood Leprosy

As childhood leprosy is a marker for activity of the disease in the community, it has to be addressed in an equally serious tone as adult leprosy. The primary source of infection in this age group is household contacts.

In children <10 years of age, the doses should be preferentially calculated according to the weight of the child, i.e., dapsone 2 mg/kg/day, rifampicin 10 mg/kg, and clofazimine 1 mg/kg/day daily and 6 mg/kg monthly [28]. The drug schedule for childhood leprosy is outlined in Table 6.5 [28].

Table 6.5 MDT regimen for childhood leprosy

Age (years)	Paucibacillary (duration: 6 months)		Multibacillary (duration: 12 months)			
	Dapsone, daily dose, unsupervised (mg)	Rifampicin, monthly dose, supervised (mg)	Dapsone, daily dose, unsupervised (mg)	Rifampicin, monthly dose, supervised (mg)	Clofazimine unsupervised (mg)	Clofazimine, monthly dose, supervised (mg)
10–14	50	450	50	450	50 every other day	150
15 or above	100	600	100	600	50 daily	300

Leprosy and Pregnancy

- None of the anti-leprosy drugs are contraindicated in pregnancy.
- Rather, early initiation of MDT to prevent fetal damage and break the chain of transmission is the primary aim of management of leprosy in pregnancy, and hence treatment is started as soon as the diagnosis of leprosy is confirmed in a pregnant woman, irrespective of the trimester [29].
- Similarly the MDT is not contraindicated in lactation; however, regular follow-ups need to be maintained with the mother and child to look for any drug-related side effects and signs of reaction.
- For leprosy reactions during pregnancy and lactation, oral corticosteroids are the mainstay of therapy along with MDT. Other than steroids, clofazimine is the preferred choice as an anti-reaction drug [29].
- Drugs like thalidomide, methotrexate, cyclosporine, and azathioprine are contraindicated.

Leprosy and Tuberculosis

- Co-infection of leprosy and tuberculosis (TB) has been predominantly reported in borderline and lepromatous disease.
- Depressed cell-mediated immunity in leprosy by a defect in Toll-like receptor 2, poor response to chemokine ligand 2, and tumor necrosis factor alpha may either reactivate latent TB or make a person vulnerable to get new infection [30].
- Further steroid use in lepra reactions and treatment of silent neuropathy may be a triggering factor in this regard.
- The potential risk of development of rifampicin resistance secondary to monthly rifampicin in leprosy is of prime concern in treating patients co-infected with TB or where diagnosis is missed initially [31].

- Hence, proper screening of all leprosy patients is compulsory, especially if there are respiratory and constitutional symptoms with abnormal chest x-ray to rule out co-infection before starting chemotherapy.
- Management of TB with concomitant leprosy remains the same as according to WHO treatment categorization with addition of dapsone and clofazimine for leprosy.

Leprosy and Human Immunodeficiency Virus (HIV)

- Co-infection of leprosy with HIV has been predominantly reported in multibacillary leprosy.
- Standard multidrug therapy along with highly active antiretroviral therapy (HAART) is the treatment of choice in all cases of leprosy with concomitant HIV.
- Moreover, early institution of HAART enhances the treatment response leading to upward shift of all clinical forms of leprosy and faster withdrawal of steroids in lepra reactions.
- Increased incidence of type 1 lepra reaction and acute neuritis is commonly observed in seropositive patients with multibacillary leprosy which are usually managed with conventional treatment for reaction in addition to HAART.
- Antiretroviral therapy leads to restoration of immunity, unmasking underlying subclinical co-infections causing immune reconstitution inflammatory syndrome (IRIS) [32]. It presents clinically as type 1 reaction with the development of erythematous, edematous skin lesions which may develop unusual ulceration and neuritis with nerve paresis/paralysis.
- Patients with CD4 cell count under 50 cells/μL, with underlying opportunistic infection, or with high microbial burden are at stake for the development of IRIS [33].
- Such patients require careful monitoring of the dose of oral corticosteroids to ensure early detection and management of opportunistic infections. Anti-inflammatory drugs and specific antimicrobial agents may also be needed along with the continuation of HAART and MDT.

Non-acceptance to Clofazimine

- Intolerance to clofazimine is mainly seen due to its gastrointestinal side effects and discoloration and darkening of the skin.
- This discoloration is generally reversible when the drug is stopped, but some patients still refuse to accept it.
- The WHO advocates the use of ofloxacin 400 mg daily or minocycline 100 mg daily as substitutes for clofazimine in such cases. It also recommends monthly administration of ROM for 24 months as an alternative treatment [34].

Dapsone Toxicity

- Dapsone toxicity can present with a wide range of clinical presentations like exfoliative dermatitis, jaundice, and some severe adverse drug reactions like hemolytic anemia, dapsone hypersensitivity syndrome, agranulocytosis, and methemoglobinemia.
- The drug is stopped immediately in such scenario with no further modifications in MB cases. However, in PB leprosy, clofazimine may be substituted for dapsone for a period of 6 months [35].
- Use of second-line agents like ofloxacin and minocycline has also been reported [36].

Hepatosafe Regimen

- Out of the three conventional drugs of multidrug therapy, rifampicin and dapsone are hepatotoxic.
- Hence, a hepatosafe regimen has been recommended by WHO for patients intolerant to the above two drugs.
- The total duration of treatment in this regime is 24 months with the initial intensive phase consisting of daily clofazimine, ofloxacin, and minocycline or clarithromycin for a period of 6 months. The maintenance consists of daily clofazimine and ofloxacin or minocycline for 18 months [37]

References

1. Hansen G, Looft C. Leprosy: in its clinical and pathological aspects. Am J Med Sci 1895;110(5).
2. Fournier M. Enterprise in botany: Van Reede and his Hortus Malabaricus–Part I. Arch Nat Hist. 1987;14(2):123–58.
3. Lowe J, Smith M. The chemotherapy of leprosy in Nigeria, with an appendix on glandular fever and exfoliative dermatitis precipitated by sulfones. Int J Lepr. 1949;17(3):181–95.
4. Pai VV, Halwai V, Rao R. Development and evolution of WHO MDT and newer treatment regimens. IAL textbook of leprosy. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2016. p. 448–63.
5. Faget GH, Pogge RC, Johansen FA, Dinan JF, Prejean BM, Eccles CG. The promin treatment of leprosy: a progress report. Public Health Rep. 1943;58:1729–41.
6. Cochrane RG, Ramanujam K, Paul H, Russell D. Two-and-a-half years' experimental work on the sulphone group of drugs. Lepr Rev. 1949;20(1/2):4–64.
7. Pettit JH, Rees RJ. Sulphone resistance in leprosy. An experimental and clinical study. Lancet. 1964;2:673–4.
8. Ji B. Treatment of leprosy. In: Mycobacteria. Boston, MA: Springer; 1998. p. 398–424.
9. Rees RJ, Pearson JM, Waters MF. Experimental and clinical studies on rifampicin in treatment of leprosy. Br Med J. 1970;1(5688):89–92.

10. Scollard DM, Adams LB, Gillis TP, Krahenbuhl JL, Truman RW, Williams DL. The continuing challenges of leprosy. Clin Microbiol Rev. 2006;19(2):338–81.
11. Cheng S, Yan B, Ma Y. Molecular basis of rifampin resistance in mycobacterium tuberculosis. Zhonghua Jie He He Hu Xi Za Zhi. 1997;20(3):183–6.
12. World Health Organization. WHO study group on chemotherapy of leprosy: chemotherapy of leprosy: report of WHO study group. WHO technical report series. 1994;847:24.
13. Chauhan D, Kamal R, Saxena A. Therapy of leprosy-present strategies and recent trends with immunotherapy. J Dermatolog Res Therapy. 2020;6(2):1–10.
14. Malathi M, Thappa DM. Fixed-duration therapy in leprosy: limitations and opportunities. Indian J Dermatol. 2013;58(2):93.
15. World Health Organization. Report of the ninth meeting of the who technical advisory group on leprosy control. WHO Regional Office for South-East Asia; 2008.
16. Ji B, Grosset J. Combination of rifapentine-moxifloxacin-minocycline (PMM) for the treatment of leprosy. Lepr Rev. 2000;71:S81–7.
17. Pattyn S, Grillone S. Relapse rates and a 10-year follow-up of a 6-week quadruple drug regimen for multibacillary leprosy. Lepr Rev. 2002;73(3):245–7.
18. Katoch K, Katoch VM, Natrajan M, Sharma VD. Chemotherapy trials in MB leprosy using conventional and newer drugs pefloxacin and minocycline. Indian J Dermatol Venereol Leprol. 2000;66(1):18.
19. Pai VV, Ganapathi R, Rao R. Development and evolution of WHO MDT and newer treatment regimens. In: IAL textbook of leprosy. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2010. p. 353–67.
20. Ji B, Accompanied MDT. (A-MDT)-more questions than answers. Lepr Rev. 2002;73:301–7.
21. Ji B, Saunderson P. Uniform MDT (U-MDT) regimen for all leprosy patients-another example of wishful thinking. Lepr Rev. 2003;74:2–6.
22. Lavania M, Nigam A, Turankar RP, Singh I, Gupta P, Kumar S, Sengupta U, John AS. Emergence of primary drug resistance to rifampicin in mycobacterium leprae strains from leprosy patients in India. Clin Microbiol Infect. 2015;21(12):e85–6.
23. World Health Organization. WHO expert committee on leprosy: eighth report. World Health Organization; 2012.
24. Rao PN, Jain S. Newer management options in leprosy. Indian J Dermatol. 2013 Jan;58(1):6.
25. Ishii N. Recent advances in the treatment of leprosy. Dermatol Online J. 2003;9(2):5.
26. Ramu G. Clinical features and diagnosis of relapses in leprosy. Indian J Lepr. 1995;67(1):45–59.
27. Kaimal S, Thappa DM. Relapse in leprosy. Indian J Dermatol Venereol Leprol. 2009;75(2):126.
28. Narang T, Kumar B. Leprosy in children. Indian J Paediatr Dermatolog. 2019;20(1):12.
29. Khanna N. Leprosy and pregnancy. In: IAL textbook of leprosy. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2016. p. 352–9.
30. Hasan Z, Jamil B, Zaidi I, Zafar S, Khan AA, Hussain R. Elevated serum CCL2 concomitant with a reduced mycobacterium-induced response leads to disease dissemination in leprosy. Scand J Immunol. 2006;63(3):241–7.
31. Nigam P, Dubey AL, Dayal SG, Goyal BM, Saxena HN, Samuel KC. The association of leprosy and pulmonary tuberculosis. Lepr India. 1979;51(1):65–73.
32. Murdoch DM, Venter WD, Van Rie A, Feldman C. Immune reconstitution inflammatory syndrome (IRIS): review of common infectious manifestations and treatment options. AIDS Res Ther. 2007;4(1):1–0.
33. Shelburne SA, Visnegarwala F, Darcourt J, Graviss EA, Giordano TP, White AC Jr, Hamill RJ. Incidence and risk factors for immune reconstitution inflammatory syndrome during highly active antiretroviral therapy. AIDS. 2005;19(4):399–406.
34. Pai VV. Second-line anti-leprosy drugs: Indian experience. Indian J Drugs Dermatolog. 2020;6(1):1.
35. Becx-Bleumink M. Relapses among leprosy patients treated with multidrug therapy: experience in the leprosy control program of the Ali Africa Leprosy and Rehabilitation Training

Center (ALERT) in Ethiopia; practical difficulties with diagnosing relapses; operational procedures and criteria for diagnosing relapses. Int J Lepr Other Mycobact Dis. 1992;60:421.
36. Guragain S, Upadhayay N, Bhattarai BM. Adverse reactions in leprosy patients who underwent dapsone multidrug therapy: a retrospective study. Clin Pharmacol Adv Appl. 2017;9:73.
37. Bhide AA, Khemani UN, Kamath RR, Vaidyanathan V, Ponathil AP, Kura MM. An alternative hepatosafe treatment in leprosy. Indian J Drugs Dermatolog. 2016;2(1):33.

Chapter 7
Counselling in Leprosy

Sunil Kumar Gupta

Abstract Counselling encourages the needy person to realize the existence of the problem and helps them to analyse the cause. Also, it helps them in finding a feasible solution. Successful counselling ends with positive change in the thought process, feelings, and activity of the patient. Leprosy is a neglected tropical disease known for stigma and discrimination of the affected. It affects the physical, psychological, social, and economic well-being of the patient. Hence, there is utmost need of counselling for the leprosy patients, their family members, and the community.

Keywords Leprosy · Counselling · Intervention in counselling

Introduction

Leprosy is a neglected tropical disease (NTD) that often results in deformity if not treated at the appropriate time. Leprosy and its deformity are best known to cause stigma and discrimination in low- and middle-income countries like India. The stigma of leprosy is a real development in many people's lives that affects their physical, psychological, social, and economic well-being. There are several causes for this damaging image of leprosy.

The Burden of Stigma and Mental Illness in Leprosy Affected

When diagnosed with leprosy, patients usually attempt to conceal the disease and try to consult from a health centre far away from their homes. Leprosy patients may withdraw communication from their spouses and/or family to avoid negative behaviour. They isolate themselves. Even community members also express their negative

S. K. Gupta (✉)
Department of Dermatology, AIIMS, Gorakhpur, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_7

attitudes by avoiding leprosy-affected people, forcing them to leave, gossiping about them, and refusing to share public transport with them. Such behaviours harm the physical, psychological, and socioeconomic status of leprosy-affected people. Psychologically, they may suffer mental stress and anxiety leading to depression and even, in some cases, suicide [1].

A multi-centric, cross-sectional questionnaire-based study was carried out in four leprosy-endemic states of India—Chhattisgarh, Maharashtra, West Bengal, and Tamil Nadu. Disease profiles like leprosy classification, deformity grade, number and size of the patches, and socioeconomic status were collected along with individual data. Of the total 220 respondents, the prevalence of depression and anxiety symptoms was 33% (73) and 19% (42), respectively. The presence of disability (47%) and female gender (46%) was significantly associated with depression. The presence of disability (32%), lower-income group (27%), and low education (22%) was significantly associated with symptoms of anxiety. As the severity of disability increased, the risk of developing depression and anxiety increased [2].

Another semi-structured questionnaire-based cross-sectional study was conducted among 358 persons affected by leprosy above the age of 18 and married who were reporting at the tertiary leprosy referral hospital, Purulia, West Bengal, India. Among the participants, 41% of them were female, 60% were aged between 18 and 45 years, 58% were literate, and 40% of the participants had a physical disability. The participants had multiple feelings of fear, anxiety, and sorrow when first diagnosed with leprosy. The majority (69%) of the participants had fear of the disease. A significant association was present among males and females feeling fear of leprosy, and the female feared more than male [3].

While both men and women were negatively affected in terms of their family and marital lives, women suffered more isolation and rejection. Psychologically, women appeared more vulnerable because they were deprived of personal contact with others in the domestic environment where they were accustomed to receiving their greatest emotional rewards. Women reported that indifference to them by other family members, or seeming negation of their presence, caused them the greatest suffering [4]. Van't Noordende et al. also found that many women affected with leprosy faced fear, abuse, and violence in their marital and sexual relationships [5].

What Does Counselling Mean

"Counselling is a helping process where one person explicitly and purposefully gives his/her time, attention and skills to assist a client to explore their situation, identity and act upon solutions within the limitations of their given environment" [1]. The GATHER (greet, ask, tell, help, explain, return visit) technique can be useful in successful counselling. Counselling services have been proven successful in reducing stigma [6].

While the scope for counselling is quite enormous, it will vary according to the specific need.

Objectives of Counselling

The objective of counselling is to encourage the needy person about the realization of the existence of the problem and help them to think and analyse the cause. Also, it helps to find a feasible solution and work on it to solve the problem. Successful counselling ends with positive change in the thought process, feelings, and activity of the client/patient (Table 7.1).

Counselling in Leprosy

Counselling in leprosy involves various levels from:

1. Leprosy-affected person
2. Family members
3. Group counselling

1. *Counselling of leprosy-affected person:* Individual counselling is required on following conditional stages of leprosy:
   (a) *Diagnosis of leprosy:* Breaking news regarding the diagnosis of leprosy is a very critical time. An empathic behaviour of a treating physician requires a good counselling technique during this stage.
   (b) *Irregularity in taking anti-leprosy treatment:* Treatment dropout is very frequent in leprosy due to the long duration of treatment and adverse cutaneous drug reaction to multidrug therapy (MDT) drugs. Adherence with MDT in the treatment of leprosy is important to minimize the risk of relapse and avoid the emergence of drug resistance [7].
   (c) *Developing reactions during therapy:* Leprosy-affected people become more depressed due to lepra reaction. This increases the chance of drug withdrawal. Both situations aggravate the rectory stage. At this time, proper counselling is required.
   (d) *Poor compliance with self-care:* Due to lack of self-care practices, leprosy patient easily develop trophic ulcers and secondary bacterial infection. Ignoring advice on self-care results in the development of disability or deformity. Regular counselling on self-care is of utmost importance for leprosy patients.

Table 7.1 Counselling process and after effects

Counselling process	Aftereffects of a good counselling
• Exploring • Understanding • Action • Interacting • Involving	• Changing how a person thinks • Changing how a person feels • Changing how a person behaves or act

(e) *Stigma and counselling:* Stigma is known to harm leprosy-affected people emotionally, socially, economically, and spiritually. A preoperative counselling session with the patients helps them reach the realistic goals that they can achieve. They should be told what benefits surgery can offer them and be made aware of the problems which will persist after the operation, such as anaesthesia and analgesia [8]. Group participants are attached with the group members and understand that they are not lonely sufferers. Sometimes role model presentations during group counselling help to raise self-esteem and increase participation in social activity.

2. *Counselling of family members of leprosy-affected people:* The family members of leprosy-affected people should be thoroughly educated about the disease course, treatment duration, lepra reaction, and infectivity. The counsellor should take care of the family image and help to cope with the disease. In the case of a woman with leprosy, her husband and in-laws should be properly counselled about how to give moral support and maintain the marital status without any unlawful act or violence.
3. *Group counselling:* Group counselling of stigmatized persons help in the common issues to more than one person at a time, encouraging the unity of sufferers, developing compassion for others, understanding the common effects of stigmatization, and beginning to overcome its harmful effects. It also helps to remove the fear of corrective surgery preoperatively [9]. Group counselling can allow those with leprosy to talk about their feelings and experiences to empower one another.

Interventions in Counselling

Counsellors provide psychological support, appropriate education, and coping skills to persons affected by leprosy. Counselling of leprosy patients is essential to enable them to cope with perceived stigma as well as managing severe enacted stigma at home, in society, place of work, or elsewhere. Counselling became more intensive in Grade 1 and for almost all in Grade 2 disability who experienced restrictions in meeting new people, participating in social activities, and indulging in socioeconomic activities. Counselling for such groups of patients required multiple approaches, including in-depth leprosy education for regular treatment, self-care measures, mobilization of coping skills, self-confidence and acceptance counselling, and follow-up counselling for those released from treatment after multidrug therapy [10].

The counselling intervention should be effective in reducing stigma, promoting the rights of people with leprosy, and facilitating their social participation.

Effective communication skills such as listening and asking effective questions were not only important but also difficult to acquire for the lay and peer counsellors.

Sharing personal experiences are highly appreciated by clients and stimulated by a deepened reflection.

The author recommends paying 20–30 min extra time to the patients with leprosy on their every visit either individually or through focused group discussion and look into the following points:

- **Integration***: Leprosy services should always be integrated into general health services. In this way, the feeling of stigma and isolation is dropped down.*
- **Education***: Breaking news regarding disease to leprosy-affected people should be in an empathetic manner. Patients with leprosy must know about the disease, its sign and symptoms, and causative agent. All the myths related to leprosy should be clearly explained to the patient. Leprosy-affected people should know the disease course and treatment duration. The patient also needs to be educated about detecting the early signs of lepra reaction. At the same time, all other family members of the patient should be screened for leprosy, and they should also be educated regarding the disease.*
- **Motivation***: Patients should be motivated regularly for self-care, compliance with proper anti-leprosy treatment, and reconstructive surgery. The patient's spouse and family members should be motivated for acceptance and normal behaviour with leprosy-affected people.*

The training involved identification of the emotions and concerns of patients when interacting socially, analysis of positive and negative social interactions, and nonverbal and verbal skills training. Role-plays, videos, and live models were used. Self-esteem and a reduction in self-perceived stigma were assessed qualitatively before and after training using semi-structured interviews.

Education-oriented counselling and psychological supportive counselling are necessary adjuncts for clinical care and treatment. Client-oriented counselling allows clients to freely express their fears and anxieties and promotes coping skills and confidence [2, 11]. The Stigma Assessment and Reduction of Impact (SARI) scale is a useful tool to assess the stigma associated with leprosy [12].

The counselling intervention is effective in reducing stigma, promoting the rights of people with leprosy, and facilitating their social participation.

All of the healthcare workers should display a good understanding of patients' difficulties and needs and acknowledge the key role of patient education. However, they express several challenges in managing patients due to lack of time, human resources, and training in patient education. |Further efforts need to be made to increase patients' general knowledge of the disease to motivate them to seek healthcare earlier and change their perception of the disease to reduce stigma. HCWs need proper training in patient education and counselling for them to acquire the necessary skills required to address the different educational needs of their patients. The counsellor should know what to do and what not to do during counselling (Table 7.2) [13].

Table 7.2 Dos and don'ts in counselling

What to do	What not to do
Great the patient on each visit	Overlook the root cause of the problem
Ask the patient about the problem that needs help	Start counselling prematurely without understanding the basic problem
Encouraging self-respect, teaching how to avoid shame, increasing self-sufficiency, working on self-regard, and explaining the importance of self-care	*Enforcing* solution/alternative on patient to solve his problem
Helping in the selection of appropriate solutions	Hurting the patient's emotion/ feelings
Explaining how to implement the solutions	Using technical and tough words for patient to understand
Regular scheduling for the next session	Time not suitable/counselling in hurry/atmosphere not conducive

Take-Home Message

- Leprosy is a chronic neglected tropical disease, often associated with stigma and prejudice.
- Leprosy-affected people develop fear, anxiety, and depression due to the disease course itself and also due to negative behaviour of the family and society.
- Women are at higher risk to develop psychological morbidity, and their marital lives are also on verge of a break.
- Counselling is an art, and for leprosy patients, it requires different stages starting from diagnosis to psychosocial rehabilitation.
- A counsellor should follow the GATHER technique on every visit by patients.
- Gradually attitudes towards leprosy are changing; however, there is still much to be done to decrease the stigma of leprosy from the community and empowerment of leprosy-affected people, especially women.

References

1. Thakor HG, Murthy P. Counselling of leprosy affected persons and the community. J Indian Med Assoc. 2004;102(12):684–7.
2. Bense N, Das P, Rao PS, John AS. Enhancing counselling strategies for leprosy patients through the participation scale. Lepr Rev. 2013;84(3):199–208.
3. Correia JC, Golay A, Lachat S, Singh SB, Manandhar V, Jha N, et al. "If you will counsel properly with love, they will listen": a qualitative analysis of leprosy affected patients' educational needs and caregiver perceptions in Nepal. PLoS One. 2019;14(2):e0210955.
4. Dadun D, Van Brakel WH, Peters RMH, Lusli M, Zweekhorst MBM, Bunders JGF, et al. Impact of socio-economic development, contact and peer counselling on stigma against per-

sons affected by leprosy in Cirebon, Indonesia—a randomised controlled trial. Lepr Rev. 2017;88(1):2–22.
5. Floyd-Richard M, Gurung S. Stigma reduction through group counselling of persons affected by leprosy—a pilot study. Lepr Rev. 2000;71(4):499–504.
6. Govindasamy K, Jacob I, Solomon RM, Darlong J. Burden of depression and anxiety among leprosy affected and associated factors—a cross sectional study from India. PLoS Negl Trop Dis. 2021;15(1):e0009030.
7. Govindharaj P, Srinivasan S, Darlong J. Perception toward the disease of the people affected by leprosy. Int J Mycobacteriol. 2018;7(3):247–50.
8. Nicholls P, Bakirtzief Z, Van Brakel W, Das-Pattanaya R, Raju M, Norman G, et al. Risk factors for participation restriction in leprosy and development of a screening tool to identify individuals at risk. Lepr Rev. 2005;76(4):305–15.
9. Ramanathan U, Malaviya GN, Jain N, Husain S. Psychosocial aspects of deformed leprosy patients undergoing surgical correction. Lepr Rev. 1991;62(4):402–9.
10. Rinehart W, Rudy S, Drennan M. GATHER guide to counseling. Popul Rep J. 1998;48:1–31.
11. Sermrittirong S, Van Brakel WH, Bunbers-Aelen JF. How to reduce stigma in leprosy—a systematic literature review. Lepr Rev. 2014;85(3):149–57.
12. Van't Noordende AT, da Silva B, Pereira Z, Kuipers P. Key sources of strength and resilience for persons receiving services for Hansen's disease (leprosy) in Porto Velho, Brazil: what can we learn for service development? Int Health. 2021;13(6):527–35.
13. Vlassoff C, Khot S, Rao S. Double jeopardy: women and leprosy in India. World Health Stat Q. 1996;49(2):120–6.

Chapter 8
Physical Rehabilitation in Leprosy

Swetalina Pradhan and Arpita Nibedita Rout

Abstract Leprosy can have long-term sequel due to nerve function impairment causing deformities. It is important to have a concise knowledge about the extent of nerve damage and the steps for prevention and correction of deformities in leprosy. We have enlisted the components of physical rehabilitation in leprosy: assessment, types, grading and monitoring of nerve function impairment along with elaboration on self-care, occupational therapy, community-based rehabilitation, splints, exercises, and reconstructive surgeries.

Keywords Deformity correction exercise and surgery · Hansen's disease Physiotherapy in leprosy · Nerve impairment in leprosy · Splints in leprosy

Introduction

Leprosy in the long term causes deformities of multiple body parts such as the face, hands, feet, and/or eyes. The deformities result in physical disabilities in the affected which hampers their everyday tasks, work, or daily earning in addition to the social stigma [1]. It is the responsibility of each and every caregiver to rehabilitate the physically disabled person to give him/her a comfortable life. Physical rehabilitation includes assessment and grading of the nerve function impairment and steps for management such as self-care, occupational therapy, community-based rehabilitation, exercises, splints, and reconstructive surgeries. In the current chapter, several components except community rehabilitation and physical rehabilitation have been discussed.

S. Pradhan (✉)
Department of Dermatology Venereology and Leprosy, All India Institute of Medical Sciences, Patna, India

A. N. Rout
Department of Dermatology Venereology and Leprosy, All India Institute of Medical Sciences, Deogarh, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_8

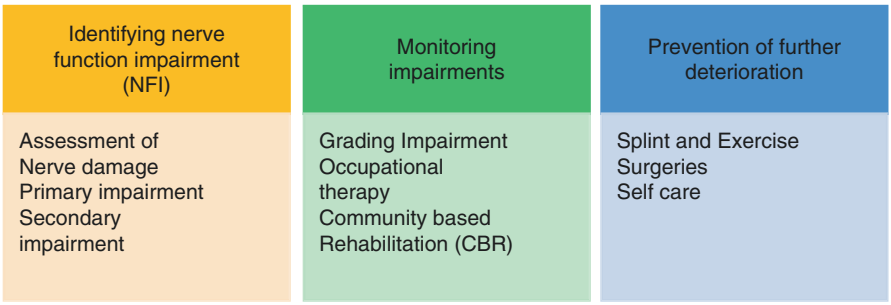

Fig. 8.1 Components of physical rehabilitation

Components of Physical Rehabilitation

Physical rehabilitation includes (1) identification of nerve function impairment, (2) monitoring impairments, and (3) prevention of further deterioration (Fig. 8.1).

Assessment of Nerve Damage

Majority of patients have already impairment in nerve function before the diagnosis of leprosy. However, once the diagnosis is done, the nerve function should be monitored at monthly intervals to see for any progression and to prevent complete loss of nerve function. It is always mandatory to take proper history of duration of impairment so that treatment can be instituted to reverse the nerve damage in case of acute onset nerve damage or impairment (<6 months duration). Both sensory and motor functions should be assessed in all cases.

The extent of nerve damage can vary from involvement of the intradermal (or feeder) nerve to the cutaneous patch to involvement of peripheral or cranial nerve trunks. The clinical manifestations can be as either silent neuropathy or loss of temperature, touch and pain sensations, motor weakness, muscle atrophy or contracture with or without nerve enlargement, and tenderness [2]. There should be at least 30% damage to the sensory fiber before there is clinical manifestation of sensory deficit. Sensory impairment can be clinically assessed by checking for sensation loss using cotton, test tubes with hot and cold water, pin prick sensation, and Semmes-Weinstein monofilaments. For assessment of motor function, the motor power grading, card test, book test (Froment's sign), pen test, and Wartenberg's sign can be looked for. Associated sympathetic fiber damage can lead to anhidrosis, which can be demonstrated with sweat iodine test. Nerve conduction studies can demonstrate decreased conduction velocity even in the absence of clinically manifest nerve damage.

Primary and Secondary Impairments in Leprosy Due to Nerve Damage

The primary impairments occur because of nerve damage in leprosy, whereas the impairments resulting out of primary impairments are called secondary (Table 8.1).

WHO grading of impairments: The WHO grading system has separate components for the hands, feet, and eyes (Tables 8.2 and 8.3).

Eye-Hand-Feet (EHF) Scoring

This scoring system takes into account the sum of the scores for the individual impairment grade for the hands, feet, and eyes to calculate the impairment sum score. The maximum sum score is 12 (2 for each of the hands, feet, and eyes) [3].

Table 8.1 Types of impairment in leprosy

Primary impairments	Secondary impairments
Face Facial nerve: Lagophthalmos Trigeminal nerve: Corneal anesthesia	Stiff joints Joint contractures Shortening Ulcers Disintegration of bones Exposure keratitis, corneal ulcer, and corneal opacity
Hand Ulnar nerve: Ulnar clawing Median nerve: Ape thumb deformity Ulnar and median nerve: Total clawing Radial nerve: Wrist drop/finger drop	
Feet Lateral popliteal nerve: Foot drop Posterior tibial nerve: Claw toes Posterior tibial nerve: Plantar anesthesia	

Table 8.2 WHO disability grades for the hands and feet

0	Absence of anesthesia and absence of any visible impairments in the hands and feet
1	Presence of anesthesia and absence of visible impairments in the hands and feet
2	Presence of visible impairment in the hands and/or feet

Table 8.3 WHO disability grades for the eye

0	No eye problems due to leprosy and no visual loss
1	Eye problems due to leprosy but vision not affected (vision is 6/60 or better; can count finger at 6 m)
2	Severe impairment to vision (vision is worse than 6/60; cannot count fingers at 6 m)

Occupational Therapy

Occupational therapy involves provision of several adaptive devices and special training to use anesthetic parts while doing daily activities along with vocational and diversional activities. Several activities of daily living like personal hygiene, brushing, bathing, feeding, and dressing as well as of work- and leisure-related activities can be done with the help of assistive technology/devices which help to compensate for the leprosy-affected person's impairments. These adaptive devices increase the affected person's sense of satisfaction and independence in carrying out routine activities and participating in social activities [4]. Special training sessions in groups are provided to the affected individuals on how to protect the affected parts while doing several daily activities like cooking, farming, tailoring, etc. The occupational therapist uses vocational activities to divert as well as to enhance the skill level of clients. The individuals are encouraged and trained for several activities such as greeting card making, candle making, carpentry, and tailoring during hospital stay which not only keep patients engaged during their hospital stays but also enhance the skills needed for their livelihoods.

Prevention of the Progression of Impairment

Some of the impairments in leprosy are irreversible due to several reasons, and in such scenarios, the goal of the rehabilitation team is to ensure the prevention of any new impairment along with the worsening of a primary impairment to a secondary impairment. The prevention part includes:

- Exercises
- Use of splints
- Surgical rehabilitation
- Self-care.

Exercises

Exercises help in improving muscle power in cases those present in early period, and those presenting late, these help in retaining the muscle bulk and tone (Table 8.4).

Table 8.4 The standard MRC (Medical Research Council) scale of muscle strength/weakness assessment [5]

Grade	Description
0	No contraction
1	Flicker or trace of contraction
2	Full range of active movement, with gravity eliminated
3	Active movement against gravity
4	Active movement against gravity and resistance
5	Normal power

The MRC grading helps in deciding the ranges and types of muscle exercises that are required for each muscle group in a patient.

If the muscle power is 0 (paralyzed) or 1 (weak), only passive exercises are recommended. For muscle power ranging from 2–3 (weak), active and active-assisted exercises are helpful. Muscles with power grades 4 (weak) and 5 (strong) need active and active-resisted exercises, respectively [6].

Exercises improve/maintain the muscle tone and bulk. Different types are listed in Table 8.5.

Table 8.5 Exercises for different group of muscles

Nerve affected	Muscle(s) affected	Exercises recommended		
		Passive	Active-assisted	Active
Facial	Orbicularis oculi	Gently pull the eyelid by placing the index finger at the lateral end of the eye so as to close the eye	Try to close the eye tightly and hold for 10–0 counts and then open × 5–10 times each hour	
Ulnar	Abductor digiti minimi, interossei, lumbricals fourth and fifth, flexor digitorum profundus fourth and fifth, flexor carpi ulnaris	Place the affected hand on a soft surface with the palm facing up and with the palm of the unaffected hand, the fingers are straightened gently, 10 times every 2–3 h, for each hand, with or without using an emollient like oil/ Vaseline	The MCP joints of the affected hand are placed at 90 ° with the wrist at neutral position and supported in this position by the unaffected hand, and the interphalangeal joints of medial four fingers are flexed and extended completely	Abduction and adduction of fingers with palms placed on flat surface; flexion and extension of the interphalangeal joints of medial four fingers with MCP joints flexed at 90 °; wrist neutral and elbow extended
Median	Abductor pollicis brevis, extensor digitorum profundus 2 and 3, opponens pollicis longus, lumbricals second and third	Opposition and abduction movement of the thumb of the affected finger with palm placed on a flat surface, hold for 5 s and repeat 10 times every 2–3 h	Flexion and extension of the interphalangeal joint of the thumb of affected hand while the MCP joint of the thumb of the affected finger is supported by the other hand	Bring the thumb of the affected hand from an extended position to the abducted position and hold for some time
Radial	Extensor carpi ulnaris, extensor carpi radialis longus and brevis, extensor digitorum communis and indicis	1. Extension of the affected wrist with the help of the other hand 2. Place the affected palm on a flat surface and lift the elbow perpendicular to the wrist, causing extension of the affected wrist joint		Extension of the affected wrist joint with the palm (facing downward) placed on the table edge, 10 repeats every 3 hours

(continued)

Table 8.5 (continued)

Nerve affected	Muscle(s) affected	Exercises recommended		
		Passive	Active-assisted	Active
Lateral popliteal	Tibialis anterior, extensor digitorum longus, extensor hallucis longus	Dorsiflexion of the affected foot by a towel looped across the plantar aspect and ends of the towel held in both hands, with sitting in leg extended position, hold the position for 10 s and release 1. Stand one foot from the wall while facing the wall, lean on to the wall, and place the hands for support, with resultant dorsiflexion of feet; 10 repeats every 2–3 h	Active dorsiflexion of the affected feet with the affected feet placed on the other lower limb in a gravity-eliminated plane	Dorsiflexion of the affected feet while sitting high with feet unsupported, hold for 15–20 s, 10 repeats every 2–3 h
Posterior tibial		Passively stretch the toes of the affected feet with the hand, with the affected leg resting on the opposite thigh and hold the position for 20 s		

Splints

Splints are supportive devices that immobilize a part of the body. There are two types of splints, dynamic splints and static splints. Static splints prevent movement of the area requiring immobilization, whereas dynamic splints allow specific movements of the immobilized area for maintaining some functions. The splints are used in neuritis and deformity correction or to keep an area in optimal position. Various types of splints and their use in leprosy are discussed in Table 8.6.

Self-Care of Anesthetic Parts

Each leprosy patient with impairment should be educated regarding care of anesthetic areas. The education should be done looking at the lifestyle and occupation of the patient for better results [7, 8]. Details of the eyes, hands, and feet are illustrated in Table 8.7.

Table 8.6 Splints and their indication

Type of splints	Indication
Ulnar neuritis slab: Extends from the back of the elbow to the palmar crease and maintains the elbow in flexion of about 60 °, providing adequate rest to the nerve	• Acute ulnar neuritis or ulnar nerve tenderness
Posterior slab/functional foot slab: Extends from the mid-calf region to the tip of the toes	• Posterior tibial neuritis or lateral popliteal neuritis • Swollen foot or leg caused by a reaction • Infected or neuropathic foot. • Supportive device for patients with foot drop or tibialis anterior weakness • Post-reconstructive surgery of foot drop to protect the transferred tendon, the tibialis posterior
Palmar slab/anterior slab/median neuritis slab: Extends from the upper second/third of the forearm to the palmar crease	• Median neuritis, whether or not muscle weakness exists • Supports the weak muscles and helps to prevent thumb web contracture
Cock up slab: Extends from the upper second/third of the forearm to the palmar crease. Maintains the wrist in extension. Paralyzed fingers are included in the splint	• Radial nerve damage associated with paralysis or weakness of the wrist extensors
Cylindrical splint: Extends from the tip to the base of the finger	• Interphalangeal joint stiffness or contracture • Finger wounds and cracks
Thumb web spica/tuck-in splint: Maintain the thumb in abducted position	• Prevent and treat thumb web contracture • Protection of the transferred tendon post-reconstructive surgery of ape thumb deformity
Functional slab for hand: It is applied with the metacarpophalangeal joint at 45 °, the proximal interphalangeal joints at 25 °, and the distal interphalangeal joint at 15 °	• Hand swelling due to lepra reaction or wound infection Gives rest to the hand in a functional position, as well as relieves pain and assists in healing
Lumbrical slab: Finger loops maintain the position of the metacarpophalangeal joint in flexion	• Maintain the hand in the lumbrical position post-tendon transfer surgery
Non-weight-bearing cast: Extends from the neck of the fibula to the tip of the toes, with the ankle joint maintained at 90 ° of dorsiflexion	• After tibialis posterior transfer surgery • Healing of simple ulcers
Below-knee cast with Bohler iron: Extends from the neck of the fibula to the tip of the toes. Bohler iron helps transmit weight and pressure to the calf area thereby preventing weight bearing on the foot	• Simple heel ulcer in a foot
Molded double rocker shoe/boot: Cast is applied below the malleoli and covers the entire foot, just like a boot	• Plantar ulcers on the forefoot

Table 8.7 Care of the hands, feet, and eyes in leprosy

Care of anesthetic hands and feet	Care of eyes
• Use thick cloth or gloves while handling hot objects to prevent burn • Use tools with wooden or rubber-covered handles to help prevent injury • Grip aids and splints to protect hands • Microcellular rubber footwear to protect feet • Soak, scrub, and smear technique: Soak anesthetic palm or sole for 20 min in cool clean water to make the skin supple. Then scrub the hard skin with a scraper stone. Smear the wet skin with oil to retain moisture and prevent dryness • Inspect the anesthetic areas daily for injuries, or even red spots, swelling, and cracks • Take adequate precautions to prevent the wound progression • Wound care at home: Clean and bandage simple wounds at home. Give rest to the wound area with adequate offloading. Report to the physician early with any evident signs of secondary infection • Change lifestyle to protect the hands and feet from being injured	Loss of corneal sensation • "Think blink" approach: The patient is taught to deliberately close the eye at regular intervals to prevent corneal damage Lagophthalmos • Wear protective eyeglasses to protect from insect, dust, injury, and dryness • Cover the head during sleep with a clean bedsheet or towel • Wear a wide-brimmed hat or cover the eye with any available cloth during the day, to prevent damage to the eye from foreign particles and insects • Do passive eye exercises to maintain muscle tone and prevent atrophy • Wash the eye with clean water at least twice a day to flush out dirt and to prevent dryness • Daily inspect the eye in a mirror to look for redness or injury • Don't rub the eye to prevent further damage

Ulcer Management

All the simple ulcers heal with the self-care practiced at home and offloading the affected area. Deep ulcers need interventions like paring/scraping or scooping followed by dressing. The non-healing ulcers require skin grafts or flaps. Some ulcers with deeper soft tissue infection and bone involvement may require reconstructive surgery.

The larger tissue defects created after excision of ulcers over the heels can be reconstructed using local rotation flap, flexor digitorum myocutaneous flap, medial plantar artery island flap, reversed sural artery flap or inferiorly based fasciocutaneous flap, and free latissimus dorsi muscle flap [9].

Similarly, forefoot ulcers and tissue defects over metatarsal heads can be managed by toe web island flap based on plantar or dorsal metatarsal supply and reversed medial plantar artery island flap, for larger defects [9].

For defects on lateral border, the flaps used are local transposition flaps, medial plantar island flap, dorsalis pedis island flap, and anterior leg flap or reversed anterior tibial artery flap.

Ulcers over the great toe can be repaired with toe web transposition flap, and for ulcers over lateral malleolus, reverse sural artery flap can be used [9].

Surgical Rehabilitation

1. Nerve surgery.
2. Reconstructive surgery.

Nerve Surgery

Common indications for nerve surgery in leprosy patients are as follows:

- Non-responsiveness or progression of nerve damage despite on corticosteroids.
- Contraindication or intolerance to corticosteroids.
- Nerve abscess.
- Intractable pain despite on adequate immunosuppressive therapy.
- Sudden paralysis.

Various types of nerve surgeries are elaborated in Table 8.8.

Reconstructive Surgery

Reconstructive surgeries are required to correct the irreversible deformities of the face and extremities along with reconstruction of soft tissue in case of contractures and large areas of tissue loss. The deformities of the hand and feet are usually dealt by tendon transfer procedure in which acting muscle is transferred to do the function of the paralyzed muscles. If the deformity is neglected and chronic resulting in fixed deformities such as a "fixed equines," "flail foot," or "rocker bottom foot," the surgical stabilization is done by using different arthrodesis procedures and then supported by specialized footwear.

Table 8.8 Nerve surgery in leprosy

Type of nerve surgery	Descriptions
Extra-neural neurolysis	Decompression surgery to release the constricting fibrous bands and ligaments and to open fibro-osseous channels 1. Ulnar neuritis: Cubital tunnel at the elbow, medial intermuscular septum, aponeurosis of flexor carpi ulnaris muscle 2. Median nerve: Carpal tunnel at the wrist 3. Radial nerve: Spiral groove of the humerus 4. Common peroneal nerve: Retro-fibular tunnel at the neck of the fibula
Intraneural neurolysis or longitudinal epineurotomy	Giving longitudinal incision in the epineurium without damaging the vasa nervorum
Interfascicular neurolysis	Dissecting and separating individual nerve bundles
Nerve abscess drainage	Longitudinal incision is given over the abscess to drain the contents
Nerve trans-positioning	Done for the ulnar nerve at the elbow to avoid stretching of the nerve with movement of the elbow joint, to increase blood supply and protect the nerve from injury

The static procedures used for correction of lagophthalmos include fascial slings to suspend the lower eyelid, loading of the upper eyelid, ear cartilage graft, median and lateral tarsorrhaphy, and tarsal strip (shortening the tarsus in the eyelids to approximate the eyelid margins to cover most part of cornea). Temporalis muscle transfer procedure or its modifications are dynamic techniques for correction of lagophthalmos.

Posterior nasal epithelial inlay skin graft and nasolabial skin flap are used for correction of nose collapse. Madarosis can be managed by free scalp graft, island pedicle scalp graft, or hair follicle implant.

Reconstructive surgeries used for ulnar clawing include transfer of palmaris longus, extensor carpi radialis longus, and flexor digitorum superficialis of the middle or ring finger. If there is associated median nerve palsy resulting in total clawing with loss of opposition and abduction movement of thumb, in addition to correction of ulnar clawing, transfer of flexor digitorum superficialis of the ring finger or extensor indicis proprius or extensor carpi ulnaris or palmaris longus has to be done.

Triple paralysis, due to damage to all three of ulnar, median, and radial nerves, requires multiple tendon transfers such as the following:

- Pronator teres (active muscle) is transferred to the extensor carpi radialis brevis to provide wrist extension.
- Flexor carpi radialis is transferred to provide four-finger extension.
- Palmaris longus is rerouted to provide thumb extension.
- Flexor digitorum superficialis of the middle finger is transferred to provide metacarpophalangeal flexion of the four fingers.
- Flexor digitorum superficialis of the ring finger is transferred for opponens plasty.

Common peroneal nerve paralysis resulting in foot drop due to loss of dorsiflexion and eversion of foot needs tibialis posterior to be rerouted to the dorsum of the foot and to be attached to the paralyzed dorsiflexors of the ankle.

For clawing of toes due to tibial nerve damaged behind the medial malleolus, the reconstructive surgery used is flexor to extensor transfer, in which for each toe, detachment of the flexor digitorum longus from its insertion and transferring it to the dorsum, and inserting the tendon into the extensor digitorum, is done.

References

1. Ganapati R, Pai VV, Kingsley S. Disability prevention and management in leprosy: a field experience. Indian J Dermatol Venereol Leprol. 2003;69:369–74.
2. Kar S, Krishnan A, Singh N, Singh R, Pawar S. Nerve damage in leprosy: an electrophysiological evaluation of ulnar and median nerves in patients with clinical neural deficits: a pilot study. Indian Dermatol Online J. 2013;4(2):97–101.
3. van Brakel WH, Reed NK, Reed DS. Grading impairment in leprosy. Lepr Rev. 1999;70(2):180–8.

4. Maia FB, Teixeira ER, Silva GV, Gomes MK. The use of assistive technology to promote care of the self and social inclusion in patients with sequels of leprosy. PLoS Negl Trop Dis. 2016;10(4):e0004644. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4849766/.
5. John J. Grading of muscle power: comparison of MRC and analogue scales by physiotherapists. Int J Rehabil Res. 1984;7:173–81.
6. Admin. 4.3 physical rehabilitation in leprosy. International textbook of leprosy. 2016. https://internationaltextbookofleprosy.org/chapter/physical-rehabilitation.
7. Cross H, Newcombe L. An intensive self-care training programme reduces admissions for the treatment of plantar ulcers. Lepr Rev. 2001;72:276–84.
8. Mathew J, Antony P, Ethiraj T, Krishnamurthy P. Management of simple plantar ulcers by home based self-care. Indian J Lepr. 1999;71:173–87.
9. Admin. 4.2 surgical aspects in leprosy [internet]. International textbook of leprosy. 2016. https://internationaltextbookofleprosy.org/chapter/surgical-aspects.

Chapter 9
Community Rehabilitation in Leprosy

Neeraj Agarwal and Abhisek Mishra

Abstract More than 80% of all newly registered leprosy cases in the world are in India, Brazil, and Indonesia combined. According to projections, even if country-level eradication is achieved by 2020, leprosy is expected to remain a concern in high-endemic areas. According to current research, almost half of leprosy patients and their families experience social, physical, or a mix of social and economic challenges, as well as debilitation or destitution. In the broadest sense, disability, which is a symptom of this disease, occurs when people are denied equitable access to resources in their families and communities. The term "rehabilitation" is often suffixed when thinking of a remedial intervention in the context of leprosy since deformities are the most obvious sign of the disease. The physical component of rehabilitation should come first, with the ultimate goal of reversing the physical consequences of leprosy, while behavioral adjustments tailored to individual patients, their families, and their cultures should come second. The case study from India highlights that the affected person is actively spreading the word about leprosy and assuring people that it is curable provided they undergo care in a timely manner. Finally, self-help groups have been found to be effective in resolving the issues that leprosy patients confront. The members of the group are well versed on the difficulties that the patient is dealing with. They learn to love, admire, and encourage one another, which builds trust and self-esteem. People can share ideas and learn from one another at group gatherings.

Keywords Discrimination · Disability · Community-based rehabilitation Integration · Empowerment

N. Agarwal (✉)
Department of C&FM, AIIMS, Bibinagar, Hyderabad, India

A. Mishra
Department of CM&FM, AIIMS, Bhubaneswar, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_9

Introduction

While India rejoices in its polio triumph, another dreaded disease, leprosy, which was eliminated in 2005, continues to haunt the country. Many that are afflicted by the condition continue to be stigmatized and discriminated against in other developing economies as well. It is well evident from the plight of a 30-year-old woman from Banki block, Odisha, which exemplifies the injustice of the stigma and myths of leprosy as reported in December 2020. Since contracting this disease, a year ago, Anita reportedly became untouchable in her village, and her family was forced to relocate to Baghamari in Khordha, about 30 km from Gholapur, where they continued to live in a rented home and struggling for a daily living [1, 2].

Multiple body parts may be involved in this disease such as the face, hands, feet, and/or eyes with characteristic deformities. The deformities result in physical disabilities that find it impossible to carry out everyday tasks, work, or earn a living. The other features include facial plaque of the non-lepromatous patient (especially if in reaction), facial palsy, claw hand deformity, foot drop, or the hypopigmented macules which are conspicuous on dark skin. The individual who is afflicted by ocular morbidity is profoundly distressed and incapacitated [2–4]. This morbidity is more severe than other impairments affecting the hands or feet, even in early stages even before it causes significant dimness of vision. Most notably, it can result in physical disabilities that find it impossible to carry out everyday tasks, work, or earn a living [2, 5, 6]. This can lower the affected person's position in their family and society, leading to psychosocial issues. From the patients' viewpoint, the disorder has an impact on many facets of their lives, including marriage, work, and social contact, especially where noticeable deformities are present.

An analysis of data on 1765 leprosy patients from the Indian Council of Medical Research (ICMR) unit for epidemiology of leprosy at Avadi, Madras, in southern India shows that paucibacillary and multibacillary patients having no impairments to begin with had about 1% and 27.3% risk, respectively, of having some impairment by the time their anti-leprosy treatment was completed [3, 7]. A recent study from Bangladesh found that paucibacillary (PB) and multibacillary (MB) patients who do not have any nerve damage before they begin multidrug therapy had 1.8% and 14.4% risk, respectively, of having nerve function impairment at the time of completion of anti-leprosy treatment. A study of 151 multibacillary cases from Delhi shows that those who had no disability when they began therapy had an 8.33% chance of experiencing any impairment 5 years later [7].

Unlike the biomedical effects, the psychosocial consequences impact not just the individuals involved but also their families. According to a survey of 500 families of two districts in South India, the proportion of families experiencing social and economic challenges has increased from 6% to 57% when the family had a leprosy patient with deformities, compared to families that had a patient without deformities. As per these studies, about 35% of leprosy patients and their families face social, physical, or a combination of social and economic challenges, as well as

debilitation or destitution [6–9]. Another big psychological challenge faced by leprosy patients is social isolation, which can be self-inflicted in many cases. In the Avadi study involving 410 persons with leprosy-related deformities, around 8% of people were found to be socially isolated, as demonstrated by not being invited to social or family events. Another research from Orissa found that 308 out of 671 leprosy patients said they were socially alienated to different degrees. Of these, only 150 (48.3%) had some leprosy-related impairments, and the other 158 (51.3%) had no impairments whatsoever [3, 4, 6, 7, 10].

Disability, the characteristic of this disease, in the broadest sense happens when people are refused fair access to resources in their families and cultures. The cultural, social, institutional, environmental, and economic barriers all exist, with attitudinal barriers being particularly important in case of leprosy. Since deformities are the most visible symptom of leprosy, the term "rehabilitation" is commonly suffixed when thinking of a remedial intervention in the context of leprosy [11, 12]. Rehabilitation is an important part of universal health coverage and is a key strategy for achieving Sustainable Development Goal 3—"Ensure healthy lives and promote well-being for all at all ages." The WHO has defined rehabilitation as "the combined and coordinated use of medical, social, educational and vocational measures for training and retraining the individual to the highest possible level of functional ability." The various rehabilitative approaches are like "medical rehabilitation" which refers to provision of anti-leprosy treatment, "surgical rehabilitation" referring to reconstructive surgery, and "physical, social, vocational, economic, and spiritual rehabilitation" which altogether enable the person to lead a meaningful life. There is also a term "preventive rehabilitation" that applies to all treatments necessary to avoid the need for further recovery [13–15].

Assessment for rehabilitation: A screening process may be done at community level to identify individuals in need of rehabilitation service as per existing health program. The frontline workers must be trained periodically for this identification and referral processes from the screening facility. Many chosen for this integration enter a process of periodic appraisal and motivation, which leads to compliance with the rehabilitation plan, which aims to acquire new life skills, social integration, and reputation restoration (Fig. 9.1).

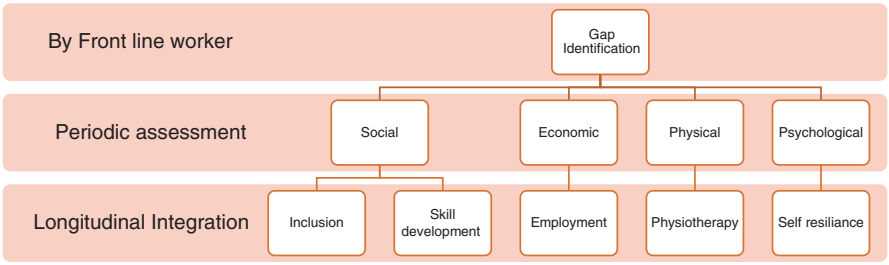

Fig. 9.1 Assessment for rehabilitation in leprosy patients

The Holistic Rehabilitation

The first point of this holistic rehabilitation is the physical component first, where the ultimate aim should be to reverse the physical effects of leprosy, while customizing behavioral changes for particular patients, their families, and their cultures should be the secondary target. The physical rehabilitation of the leprosy-affected has been discussed in the previous chapter.

The International Labor Organisation (ILO), United Nations International Children Emergency Fund (UNICEF) and World Health Organisation (WHO) have both come up with the following concept of community-based rehabilitation (CBR) which is defined as "a strategy within general community development for the rehabilitation, equalization of opportunities, and social inclusion of all people with disabilities" [15]. CBR's main objective is to help communities take steps to ensure that people with disabilities have the same benefits and resources as anyone else (Fig. 9.2).

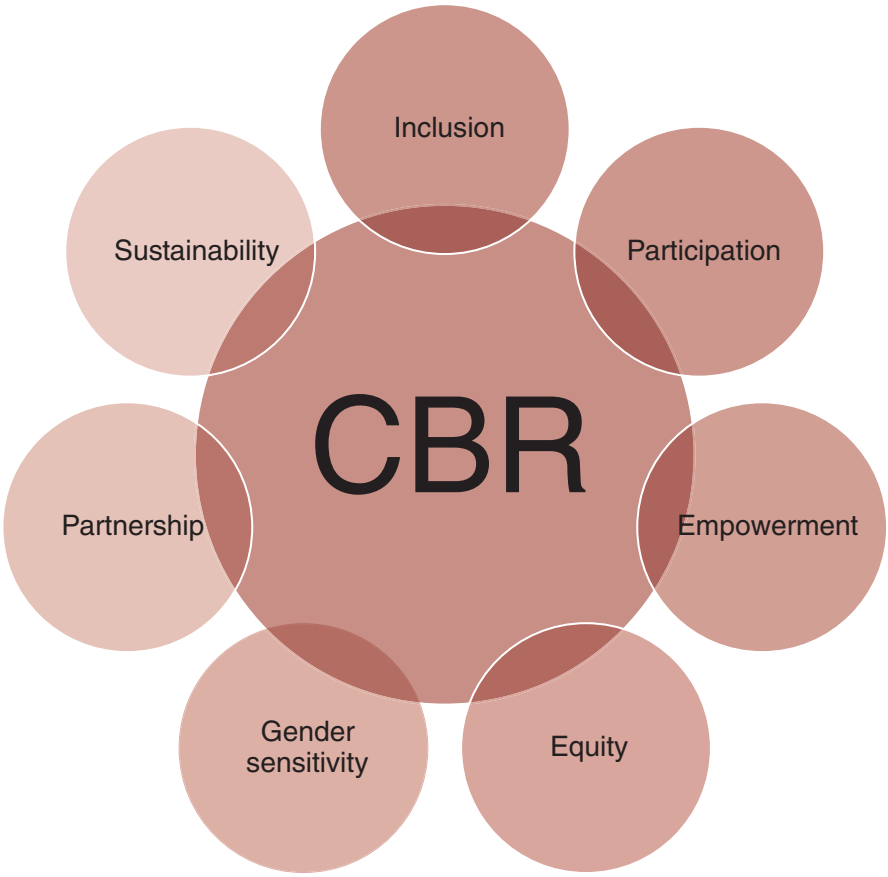

Fig. 9.2 Components of the community-based rehabilitation in a nutshell

Case Study from India

Beeramma is 40 years old. She used to be a decent singer when she was younger, and the villagers would ask her to sing devotional songs at festivals and other special occasions. She found patches on her neck about 20 years earlier, and doctors convinced her she had leprosy. She started the medication, but the pills left her ill, so she stopped taking them. She started to lose sensation in her hands and legs over time, and she developed disabilities. When CBR workers visited her village, they noticed that Beeramma kept away from other people. When they asked why she wouldn't join like the rest, she said she was frightened of being humiliated because of her impairment and leprosy. She said "When people tease me, I am really hurt." The staff counseled her and persuaded her to join a new village self-help community. Beeramma agreed to join the group and became one of its leading members. She learned to secure her hands and feet and is now occupied with housework and sheep care. There is no stigma towards her in the community. Looking back, she says "For a long time I lived within four walls. I kept myself apart. Now I realize that people do not think badly of me. I was the one who had an inferiority complex. Now I realize that no one is without value." Beeramma is also actively spreading the word about leprosy and assuring people that it is curable provided they undergo care in a timely manner.

Social Support from Self-Help Groups and in the Form of Microcredits

All the components of the CBR are overlapping with community engagement and social support at its core. The social support mechanism must be put in place not only for leprosy patients but also for other forms of disability [16–18]. Hence, instead of simply including people with leprosy, these groups can include people with a wide range of disabilities in the mainstream by self-help groups. Microcredit loans with a decent and sustainable interest rate have proven to be an efficient way to raise revenue and foster empowerment and self-resilience [9, 18, 19].

Self-help groups have been shown to be successful in a variety of areas in solving the purpose. The members get together on a daily basis to talk about and share issues. They develop trust and self-esteem by learning to love, appreciate, and inspire one another. Group meetings enable people to exchange ideas and learn from one another [20–22]. The existing members assist in needs and skills assessments with new members and may review rehabilitation plans of others. Increased social visibility of group members aids in changing views and encouraging recognition. When members talk as a group, locals and officials are more inclined to listen. Formalizing a group's legal status will help them gain access to political and financial resources. It becomes easier to integrate a small and committed community into conventional self-help groups. As a result, equality and engagement as equal members of the society were promoted [21, 23].

Case Study from India

Sakti the Self-Help Group: In Pallathur, a self-help group with eight people affected by leprosy is being created by the team from the World Health Organization. The WHO team has informed them and their families of the benefits of self-help groups, but the families declined to participate. They did not understand how it would work. People with leprosy-related illnesses, they believed, needed to be supported during their lives. The team held regular meetings, but there was always the question "What do we get out of it?". Then the team had identified eight other people with different forms of disability. One had a physical disability, some were blind, and some had speech or hearing problems. The team had encouraged all 16 people to join in an integrated self-help group. They all agreed, though it took 1 year for the clients and their families to understand the concept. They called the group Sakti, meaning power. They now meet every 2 weeks, and there is no longer any stigma between them. They try to understand each other's problems. When the group was recognized by the government, it was awarded RS 25,000 as a revolving fund, so it is now financially secure.

Another component of self-help and social support is the microcredit programs. It is a social support mechanism where a small amount of loans may be disbursed to the needy as per its financial terms and conditions. A microcredit program is different from a program that is making grants or charity. This loan program must be conducted on commercial terms, with very straightforward terms and simple accounting processes that all members understand [20, 23]. Monitoring of repayments should be included among agreed procedures. It is unrealistic to expect one person to refund the money given to them while another is entitled to have it. The image below has been identified as being important for running a successful microcredit program (Fig. 9.3).

A Delhi-based NGO, Sasakwa-India Leprosy Foundation (SILF), aims to provide available jobs for those who have been impacted by it and their families. Its main focus is on people living in segregated colonies [22]. During 2015–2016, its livelihood program empowered 2044 families, across 18 states in India, in trades such as goat and cow rearing, coir rope making, cutlery making, etc.

Case Study from Odisha

"The women with the Yellow Sarres" The Coir Rope Enterprise, Shantidan Leprosy Colony, Khurda, Odisha. This is an all-women's enterprise for making coir ropes. In 2010, SILF signed off financial support to these women to take over an already running small-scale plant making coir rope. Prior to taking over this factory, all five women relied on low daily pay and part-time work to make ends meet. Their goal was to expand the small factory, which produced rope with basic, manual equipment, to a larger facility that used an electric machine. The strategy was well thought out, and the beneficiaries were enthusiastic; however, achieving their goals was not

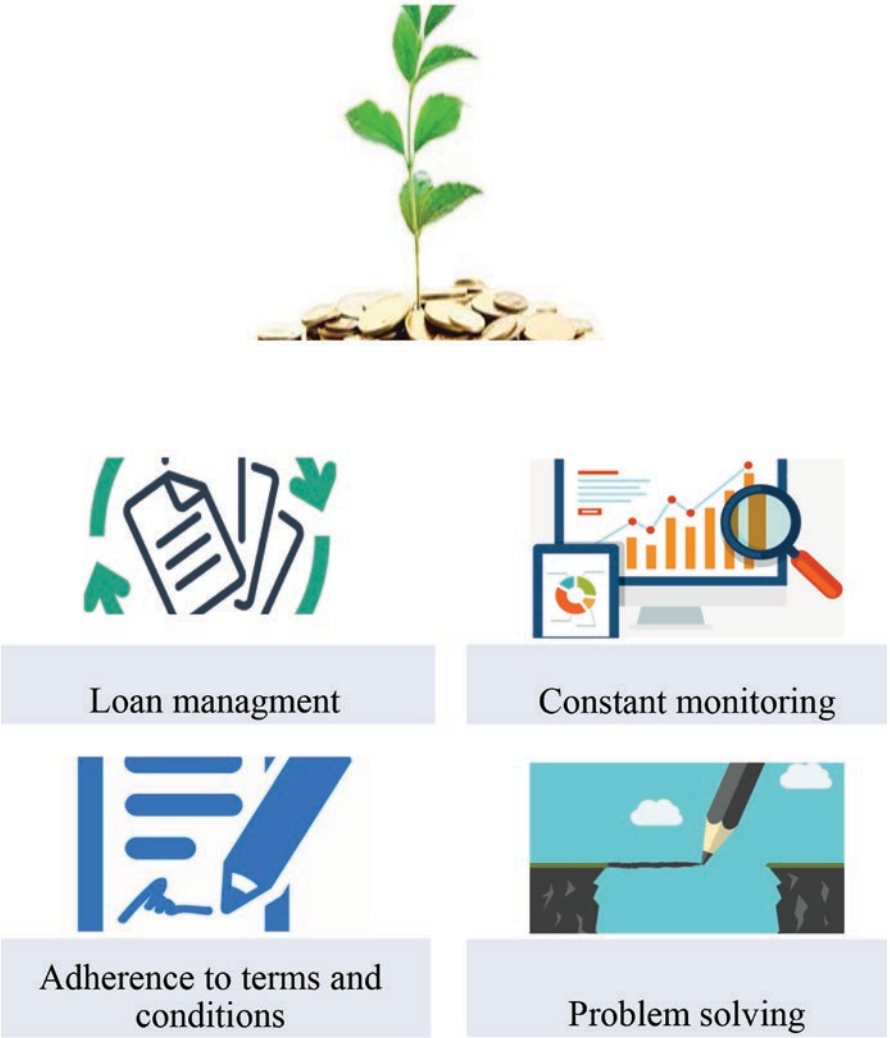

Fig. 9.3 Microcredit programs for rehabilitation in leprosy

as simple as they had expected. With the support of SILF, People's Forum, and their colony leader, these women went to the authorities and convinced them to mount a transformer in the colony. This was a significant move forward, but their trip was far from over. Today the enterprise is well established and profitable, producing more than 50 kg of rope daily. The women's pride in their profession is evident in their optimism and smiles as they arrive at work in their brilliant yellow saris, which they choose for themselves.

In a revamped effort to reduce cases, the government of India recently announced a slew of measures to widen population screening and carry out regular surveillance of this disease. The MoH&FW released operational guidelines in December 2020 that prescribe annual or bi-annual screening instead of occasional campaign drives. Screening has been proposed once a year in areas with prevalence rates lower than 1 per 10,000 populations and twice a year in areas with higher rates. ASHA workers have been contributing to early leprosy case detection across India. They visit house to house to identify people with signs and symptoms of leprosy and refer them to the nearest government health facility for confirmation. Lack of public awareness about leprosy is one of the major problems that India is facing in its efforts against the disease. Screening has been proposed once a year in areas with prevalence rates lower than 1 per 10,000 population and twice a year in areas with higher rates.

Way Forward

Early case detection, regular and complete treatment, and early detection of impairment and disability will play a pivotal role in reducing the disease and disability burden in the community. The challenge is to tackle the research gaps through novel collaborations, to improve operational aspects of the national programs. The medical curriculum needs to be revamped where there is a need to reintroduce leprosy with much focus on mainstreaming of the patients and their rehabilitation. In addition, we must educate children about leprosy in primary schools in order to instill in them the awareness that leprosy is a curable and non-infectious disease. This will help address the problem of discrimination of patients in the society. The legislation and (new inclusive) policies of great importance are themselves to be put in motion for the protection, promotion, and rehabilitation of the disabled person.

As practitioners, we must collaborate closely, particularly with those who lack access to care: those who are unaware of their rights and who often need and want health, social, occupational, and educational services for themselves. To strengthen the functioning of national leprosy services and the feasibility of partnerships with long-term collaborators, implementation analysis is needed. Support organizations providing peer counseling, peer-to-peer networks led by local professionals, social growth, and the participation of people affected in leprosy are there, but it needs to be standardized nationally and internationally. It is equally relevant to increasing the quality of leprosy data that's being generated through existing systems. The strengthening of the public health system at the ground level is necessary to handle this issue in areas where a large number of cases are being reported. An awareness campaign to deal with stigma and discrimination is also necessary so that those infected come forward for treatment and don't feel left out.

References

1. Family ostracised over leprosy stigma in Odisha, rescued. The new Indian express. 2020. https://www.newindianexpress.com/states/odisha/2020/dec/16/family-ostracised-over-leprosy-stigma-in-odisha-rescued-2236947.html. Accessed 14 April 2021.
2. WHO. Global leprosy (Hansen disease) update, 2019: time to step-up prevention initiatives. WklyEpidem Rec. 2019b;2020(95):417–40.
3. Srinivas G, Muthuvel T, Lal V, Vaikundanathan K, Schwienhorst-Stich EM, Kasang C. Risk of disability among adult leprosy cases and determinants of delay in diagnosis in five states of India: a case-control study. PLoSNegl Trop Dis. 2019;13:e0007495.
4. Singh R, Singh B, Mahato S. Community knowledge, attitude, and perceived stigma of leprosy amongst community members living in Dhanusha and Parsa districts of southern Central Nepal. PLoSNegl Trop Dis. 2019;13:e0007075.
5. Galhotra A, Panigrahi SK, Pal A. Leprosy—a raging persistent enigma. J Family Med Prim Care. 2019;8:1863–6.
6. Katoch K, Aggarwal A, Yadav VS, Pandey A. National sample survey to assess the new case disease burden of leprosy in India. Indian J Med Res. 2017;146:585–605.
7. H. Srinivasan. The problem and challenge of disability and rehabilitation in leprosy. Asia Pac Disabil Rehabil J. 1998;9(1).
8. Thappa DM, Kaur SM, Sharma VK. Disability index of hands and feet in patients attending an urban leprosy clinic. Indian J Lepr. 1990;62:328–37.
9. Rao PN, Suneetha S. Current situation of leprosy in India and its future implications. Indian Dermatol Online J. 2018;9(2):83–9. https://doi.org/10.4103/idoj.IDOJ_282_17.
10. Tiwari A, Blok DJ, Arif M, Richardus JH. Leprosy post-exposure prophylaxis in the Indian health system: a cost-effectiveness analysis. PLoSNegl Trop Dis. 2020;14(8):e0008521. https://doi.org/10.1371/journal.pntd.0008521.
11. Correia JC, Golay A, Lachat S, Singh SB, Manandhar V, Jha N, et al. "If you will counsel properly with love, they will listen": a qualitative analysis of leprosy affected patients' educational needs and caregiver perceptions in Nepal. PLoS One. 2019;14:e0210955.
12. Sardana K, Bhushan P, Khurana A. Chemotherapy. In: Sardana K, Khurana A, editors. Joplings handbook of leprosy. 6th ed. New Delhi: CBS Publishers; 2020.
13. Smith CS, Aerts A, Kita E, Virmond M. Time to define leprosy elimination as zero leprosy transmission? Lancet Infect Dis. 2016;16:398–9.
14. WHO. Global leprosy strategy 2016–2020. Accelerating towards a leprosy-free world. Geneva: World Health Organization; 2016a.
15. Global Partnership for Zero Leprosy. GPZL reports on research priorities. Lepr Rev. 2019;90:237–89.
16. Scollard D, Gillis T. International textbook of leprosy. 2020. https://internationaltextbookofleprosy.org/. Accessed 2 April 2021.
17. Khazai Z, Van Brakel W, Essink D, Gillis T, Kasang C, Kuipers P, et al. Reviewing research priorities of the leprosy research initiative (LRI): a stakeholder's consultation. Lepr Rev. 2019;90:3–30.
18. Alami H, Gagnon MP, Fortin JP. Digital health and the challenge of health systems transformation. Mhealth. 2017;3:31.
19. Simpson H, Quao B, van der Grinten E, Saunderson P, Ampadu E, Kwakye-Maclean C, et al. Routine surveillance data as a resource for planning integration of NTD case management. Lepr Rev. 2018;89:178–96.
20. Yotsu RR. Integrated management of skin NTDs—lessons learned from existing practice and field research. Trop Med Infect Dis. 2018;3:120.
21. Galhotra A., Mishra A. Neglected tropical diseases: a biosocial perspective. In: Singh P. (eds) Infectious diseases and your health 2018. Springer, Dermatol Sin https://doi.org/10.1007/978-981-13-1577-0_9.

22. Nurturing sustainable livelihoods. Sasakawa India Leprosy foundation. 2021. https://silf.in/nurturing-sustainable-livelihoods/. Accessed 11 March 2021.
23. WHO. WHO/ILEP technical guide on community-based rehabilitation and leprosy. World Health Organization. 2007.

Part II
Case Studies

Chapter 10
Annular Erythematous Plaque on the Face in a Lady

Rajesh Kumar Mandal

Abstract Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* and is broadly divided into tuberculoid and lepromatous poles. Tuberculoid leprosy is characterized by a few well-defined hypopigmented macules or plaques with sensory loss. There may be adjacent nerve involvement. Presence of acid-fast bacilli in slit skin smear or tissue sample is confirmatory. Treatment is based on multidrug therapy (MDT). Here we report a case of tuberculoid leprosy in a 34-year-old woman.

Keywords *Mycobacterium leprae* · Tuberculoid leprosy

Clinical Presentation

A 34-year-old woman presented with a well-defined reddish patchy eruption over her right cheek for 6 months. The lesion was increasing slowly. She also states that she has no sensation over the affected area. On cutaneous examination, an oval hypopigmented plaque of 8 × 6 cm diameter was seen on her right cheek (Fig. 10.1); the margin was well defined, erythematous, and raised; and the surface of the lesion was xerotic. There was decreased pin pricking sensation over the lesion comparable to the opposite side. The fine touch and temperature sensations were intact over the lesion. Superficial cutaneous nerves adjacent to the lesion like supraorbital, infraorbital, zygomatic branch of the facial nerve, supratrochlear, and greater auricular nerves were not palpable. There was no lymphadenopathy.

R. K. Mandal (✉)
Department of Dermatology, North Bengal Medical College, Darjeeling, West Bengal, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_10

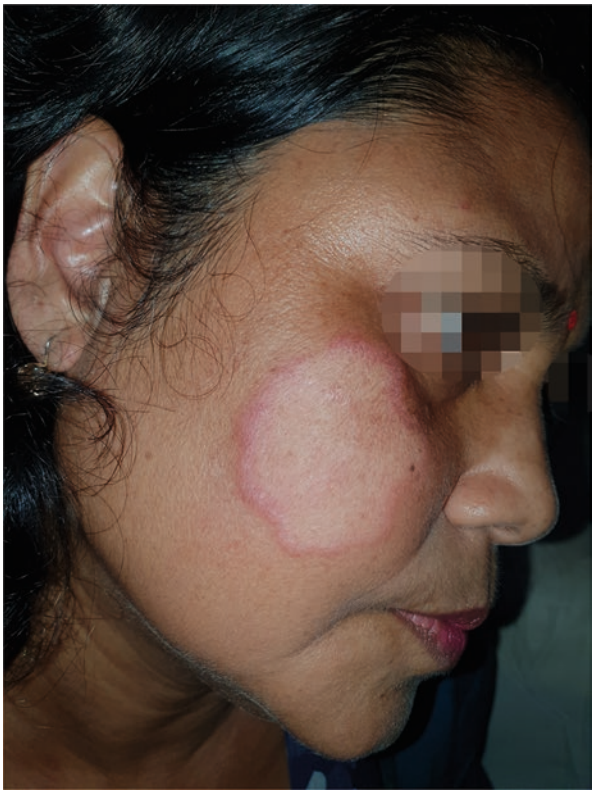

Fig. 10.1 Well-defined annular plaque with raised erythematous border and central hypopigmentation

What Is Your Diagnosis?

- Hansen's disease (TT).
- Granuloma annulare.
- Sarcoidosis.
- Lymphoma.

Investigations

A slit skin smear done from both earlobes; eyebrows and the lesion did not yield any bacilli. A punch biopsy was taken from the lesion, and the histopathological examination showed epidermal thinning. There were numerous elongated granulomas in superficial and deep dermis. The granulomas were periadnexal and perivascular mainly. The granulomas consisted of epithelioid cells, Langhans giant cells, lymphocytes, and occasional polymorphonuclear cells (Fig. 10.2a, b). Result of Ziehl-Neelsen staining was negative.

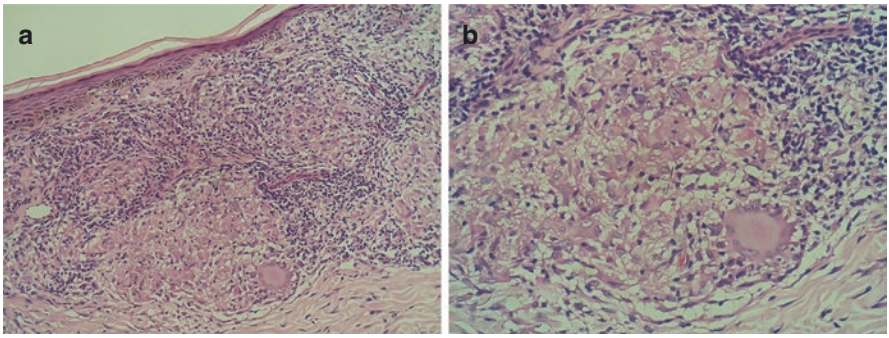

Fig. 10.2 (**a**) Thinned epidermis and well-formed epithelioid granuloma in the upper dermis (H&E ×100). (**b**) Granuloma consisting of Langhans giant cell and epithelioid cells. Lymphocytes can be seen at the periphery of the granuloma (H&E ×400)

Final Diagnosis

With the above clinical and histological findings, a diagnosis of tuberculoid leprosy was made.

Discussion

Tuberculoid leprosy (TT) is characterized by five or less lesions. There may be well-defined, hypopigmented or erythematous macules or plaques. Sometimes the lesional margin may be elevated with inward sloping. There is sensory impairment over the lesion with decreased or absent pain, fine touch, and temperature sensation. Any body part may be affected, but uncovered body parts may be involved more frequently [1]. As the autonomic nerves may get involved, the surface of the lesions may be xerotic due to decreased sweating. There may be loss of hairs over the lesions. One or two adjacent nerves may get involved and may become thickened.

As the disease further progresses, a more unstable borderline (BB) appears with more lesions and nerve thickening. Towards lepromatous pole (LL), the bacilli are widely distributed with innumerable lesions and nerve involvement. The skin and peripheral nerves are widely infiltrated with the bacilli.

Slit skin smear (SSS) is usually positive in cases with high bacterial load as in lepromatous pole (LL). In a tuberculoid pole, the bacterial load is less so the chances of getting acid-fast bacilli (AFB) in smears are also grim. In TT, demonstration of bacilli is not possible due to low bacterial load [2].

Histopathologically, TT is characterized by non-caseating epithelioid cell granuloma. The granulomas are typically centered around cutaneous nerves. Sometimes the granuloma may be of serpentine shape as it follows the nerve. The epidermis may be normal, or atrophic. There is absence of the grenz zone. The granuloma may

involve the dermis and subcutaneous fat. The granulomas usually have Langhans giant cells with numerous lymphocytes. There is scarcity of bacilli in TT [3].

Histopathological examination usually helps to confirm doubtful cases and also helps to observe treatment outcome of the disease following therapy [4]. Sarcoidosis, granuloma annulare, and granulomatous rosacea may sometimes be confused histologically with TT leprosy. In sarcoidosis, there is naked granuloma as the lymphocytes are few. There may be mild dermal fibrosis. In granuloma annulare, there is palisading granuloma with necrobiosis and mucin deposition. In granulomatous rosacea, the granulomas are lymphocyte dominant and are centered around the pilosebaceous units, and there may be plasma cells.

Treatment of TT is based on MDT. As per WHO guidelines (2018), a three drug regimen consisting of rifampicin, dapsone, and clofazimine should be given for 6 months. Prognosis of TT is very good, and sometimes the lesion may heal itself without any medication. Chances of deformity are also very less [4].

References

1. Imbiriba EB, , Hurtado-Guerrero, Garnelo L. Epidemiological profile of leprosy in children under 15 in Manaus (Northeren Brazil), 1998-2005. Rev Saude Publica 2008;42:1021–26.73.
2. Lucus SB, Ridley DS. The use of histopathology in leprosy diagnosis and research. Lepr Rev. 1989;60:257–62.
3. Kumar B, Dogra S. Case definition and clinical types of leprosy. In: Kumar B, Kumar KH, editors. IAL textbook of leprosy. 2nd ed. Jaypee Brothers Medical Publishers (P) Ltd; 2016. p. 236–53.
4. Guidelines for the diagnosis, treatment and prevention of leprosy. WHO; 2018. https://apps.who.int/iris/bitstream/handle/10665/274127/9789290226383-eng.pdf. Accessed 21 Oct 2021.

Chapter 11
27-Year-Old Male with Hypopigmented Patch on the Left Thigh

Swetalina Pradhan

Abstract The classical morphological presentation of borderline tuberculoid leprosy is hypopigmented, anaesthetic/hypoaesthetic patch with regular to irregular border, pseudopodia-like extension and has satellite lesions. The patches are of large size and can be up to 20 cm. Though the number of skin lesions is less in number, the patients are prone for type 1 lepra reaction and neuritis. In the present chapter, we are describing a classical case of borderline tuberculoid leprosy without any lepra reaction and disability.

Keywords Borderline tuberculoid leprosy · Satellite lesion · Ichthyosis · Anaesthesia · Asymmetry · Neuritis

Clinical Presentation

A 27-year-old male presented with hypopigmented, anaesthetic patches over the lower extremities and trunk for 7 months. He initially noticed the hypopigmented patch over the left thigh, and subsequently two new patches appeared over the left arm and leg over 4 months. Father of the patient had leprosy and was on treatment with MDT MB adult for 8 months. On close examination, there were hypopigmented patches of size ranging from 4 × 5 cm to 6 × 8 cm with regular to irregular margin, pseudopodial extension, and satellite lesions (Fig. 11.1). The patches were dry with ichthyotic changes. There was relative loss of hair over the patches compared to the surrounding area and loss of sensation to light touch ranging 80–90%. Left ulnar nerve was enlarged and non-tender.

S. Pradhan (✉)
Department of Dermatology, AIIMS, Patna, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_11

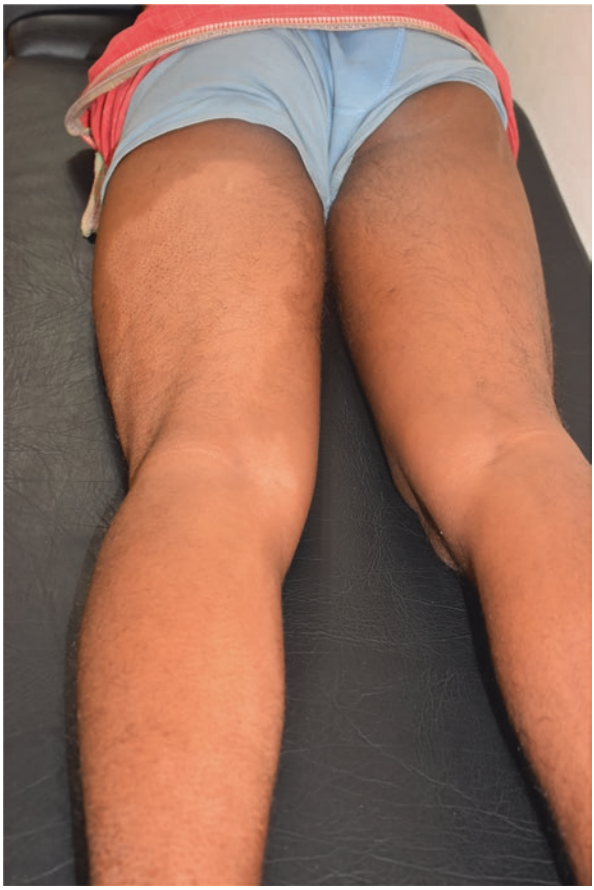

Fig. 11.1 Large hypopigmented patch with xerotic surface and reduced hairs

What Is the Diagnosis?

1. Borderline tuberculoid leprosy.
2. Hypopigmented mycosis fungoides.
3. Post kala azar dermal leishmaniasis.
4. Vitiligo.

Investigations

His routine haematological parameters were within normal limits. Slit skin smear for AFB from the ear lobes, active lesion was positive with bacillary index 1+. Histopathology from the lesion revealed epithelioid cell granuloma in a branching pattern, following the neurovascular bundle. A clear sub-epidermal zone free of any inflammatory cells (grenz zone) was seen (Fig. 11.2a, b).

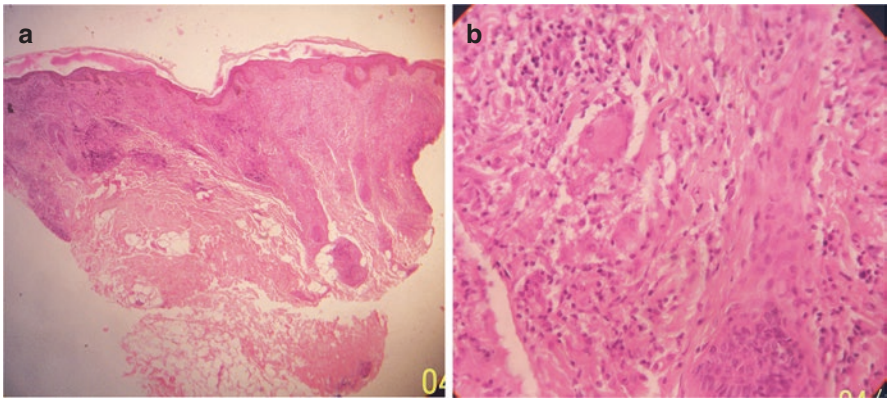

Fig. 11.2 (**a**) Well-formed periappendageal granuloma in the upper and mid-dermis with grenz zone (H&E ×100). (**b**) Langhans giant cell and epithelioid cell granuloma (H&E ×400)

Final Diagnosis

Borderline tuberculoid leprosy.

Discussion

Leprosy is classified within two poles of the disease with transition between the clinical forms [1]. Based on clinical, histopathological, and immunological criteria, it has been divided into five forms: (1) tuberculoid polar leprosy (TT), (2) borderline tuberculoid (BT), (3) mid-borderline (BB), (4) borderline lepromatous (BL), and (5) lepromatous polar leprosy (LL). For therapeutic purpose, the patients were initially divided into two broad groups: paucibacillary (TT, BT) and multibacillary (mid-borderline (BB), BL, LL) [2]. However later on the classification changed according to the number of skin lesions, less than or equal to five for paucibacillary (PB) and greater than five for the multibacillary (MB) form.

Morphologically BT leprosy presents as hypopigmented, anaesthetic/hypoaesthetic patch with regular to irregular border, pseudopodia-like extension and has satellite lesions. The patches are of large size and can be up to 20 cm [3]. The number of lesions vary from 3 to 10. The lesions have asymmetrical distribution. Common sites involved are the face, lateral aspects of the extremities, buttocks, and scapulae. The surface of lesions is dry and scaly and looks bright and infiltrated. The hair growth over the patches is markedly diminished [3]. There is nearly 80–90% loss of sensation to temperature and light touch on the lesions. There can be loss of sensation along the distribution of an involved cutaneous nerve or nerve trunk on the extremities. Asymmetrical enlargement of peripheral nerve trunks is found. Sometimes the enlarged feeder nerve (nerve supplying the affected area) can be

found in the vicinity of a hypopigmented patch. Slit skin smear for AFB usually done from ear lobes, active lesion is usually positive with bacillary index: 1+ to 2+. Histopathology from the lesions shows epithelioid cell granuloma in a branching pattern, following the neurovascular bundle. The number of lymphocytes is lesser than that of tuberculoid leprosy [4]. Infiltration of the nerve is typically seen with few AFB [BI 0–2]. Perieccrine and periappendageal (arrector pili) can be seen. A clear sub-epidermal is always found. The medical treatment for BT leprosy is WHO multidrug therapy (MDT PB) if the number of lesions is ≤5 and if there is a single nerve enlargement. However, recently even if the number of lesions is five or less, single peripheral nerve enlargement is an indication for starting WHO MDT MB regimen. Patients should be counselled for hand and feet care in case of loss of sensation over extremities and regarding the drug side effects for treatment compliance and follow-up.

Without treatment, the BT Hansen patient can downgrade to borderline lepromatous or subpolar lepromatous leprosy with passage of time. In such cases, the patient will have lesions of large (BT lesions) and small size (BL or LL lesions).

BT patients usually present with type 1 lepra reaction in which the old BT lesion will become erythematous and edematous along with appearance of new lesions. There can be associated neuritis and/or sudden onset neurological deficit like wrist drop, claw hand, or foot drop. The neuritis should be treated earliest with a high dose of corticosteroid (1–1.5 mg/kg BW) to arrest the ongoing nerve damage and regain of neural function. The treatment should be started within 6 months of onset of neural deficit for recovery of neural function [2, 3].

BT lesions over face usually persist for long, and it is difficult to appreciate anaesthesia due to overlapping nerve supply and hence diagnosed late. Type 1 reaction over face affecting facial nerve can lead to facial palsy and lagophthalmos. Apart from this, the patient can have persistent and recurrent type 1 reaction on the BT lesions over the face [5].

In our case, the patient presented early as one of his family members had already leprosy. The patient had no evidence of lepra reaction. He was started with WHO MDT MB regimen as there was nerve enlargement.

References

1. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five-group system. Int J Lepr Other Mycobact Dis. 1966;34(3):255–73.
2. Eichelmann K, González González SE, Salas-Alanis JC, Ocampo-Candiani J. Leprosy. An update: definition, pathogenesis, classification, diagnosis, and treatment. Actas Dermosifiliogr. 2013;104(7):554–63.
3. Fischer M. Leprosy–an overview of clinical features, diagnosis, and treatment. J Dtsch Dermatol Ges. 2017 Aug;15(8):801–27.
4. Maymone MBC, Laughter M, Venkatesh S, Dacso MM, Rao PN, Stryjewska BM, Hugh J, Dellavalle RP, Dunnick CA. Leprosy: clinical aspects and diagnostic techniques. J Am Acad Dermatol. 2020;83(1):1–14.
5. Reibel F, Cambau E, Aubry A. Update on the epidemiology, diagnosis, and treatment of leprosy. Med Mal Infect. 2015;45(9):383–93.

Chapter 12
Erythematous Plaque on the Lower Face

Sanjeev Gupta and Saurabh Swaroop Gupta

Abstract A 55-year-old female presented to our outpatient department with an erythematous plaque on the lower side of the face and upper lip for 8–9 months. On examination, sensations were intact, and no peripheral nerves were palpable. All the routine investigations were within normal limits. Skin biopsy was done which confirmed the diagnosis of borderline tuberculoid leprosy with 1+ bacillary index. Patient was treated with MB-MDT regimen along with supportive treatment.

Keywords Leprosy · Borderline tuberculoid leprosy

Clinical Presentation

A 55-year-old female, housewife, and a resident of Saharanpur (Uttar Pradesh) presented with raised, erythematous plaques on the lower side of the face (chin) and upper lip for the last 8–9 months. The lesions were mostly asymptomatic barring some tingling sensation intermittently; lesions showed gradual progression in size and shape without any history of regression of the lesion or spontaneous remission. There was no apparent loss of sensation over the lesions. Patient had no history of similar lesions previously, no significant family history, and no history of diabetes, hypertension, and other comorbidities. On examination, ulnar and peroneal nerves showed no apparent thickening or tenderness, and feeding nerve to the lesion was not distinctively palpable. Motor examination was normal, and the sensory examination was inconclusive. On physical examination, the plaques were edematous, non-tender, with ill-defined margins, measuring 8 × 6 cm present over the chin and right lower side of the cheek, and 5 × 2 cm involving the upper lip (Fig. 12.1a, b). Submandibular, posterior auricular and cervical lymph nodes were palpable

S. Gupta (✉) · S. S. Gupta
Department of Dermatology, Maharishi Markandeshwar Institute of Medical Sciences and Research Mullana, MMDU, Ambala, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_12

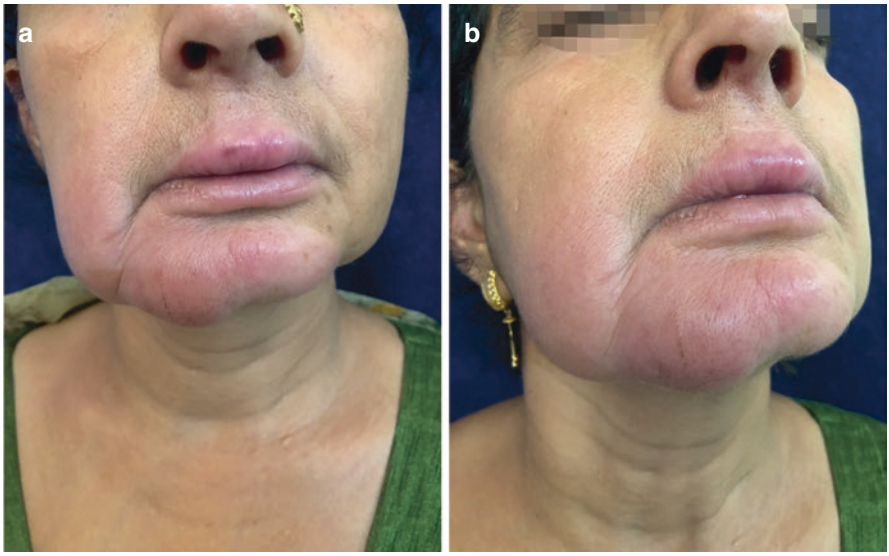

Fig. 12.1 (**a** and **b**) Erythematous plaque on the lower face involving the lip

within normal limits and were non-tender. No hepatosplenomegaly was detected on physical examination. Oral cavity was normal.

What Is Your Diagnosis?

1. Hansen's disease
2. Sarcoidosis
3. Leishmaniasis
4. Lupus vulgaris
5. Lymphocytoma cutis
6. Jessner's lymphocytic infiltrate

Investigations

All routine blood investigations were within normal limits, chest x-ray PA view was normal, angiotensin-converting enzyme levels were within normal limits, and serum calcium was also normal. Peripheral blood smear examination was negative for LD bodies. Mantoux test was negative, which along with normal chest x-ray findings ruled out lupus vulgaris. Slit skin smear was done from the lesion which was negative for AFB (lepra bacilli) and LD bodies. Skin biopsy was taken from the lesion which on histology showed a well-defined epithelioid cell granuloma with a

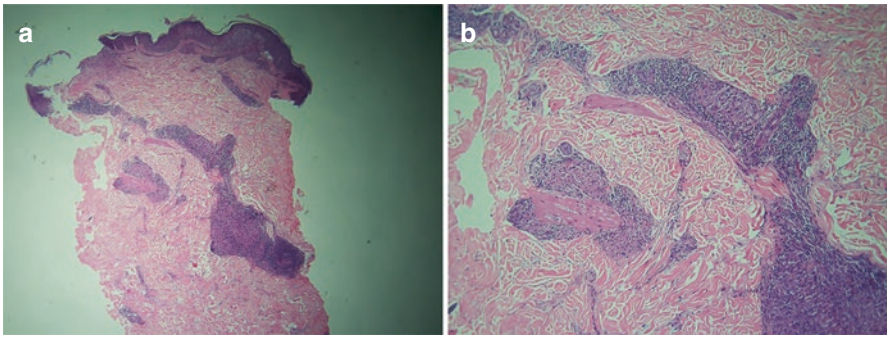

Fig. 12.2 (**a**) Curvilinear granuloma in the upper and deep dermis (H&E ×40). (**b**) Granuloma around the nerve and arrector pili muscle (H&E ×100)

moderate number of lymphocytes located mainly around the dermal nerves (Fig. 12.2a, b). Perineural and perivascular lymphocytic infiltration was noted along with a few lepra bacilli on ZN staining (bacillary index 1+).

Final Diagnosis

Borderline tuberculoid leprosy without any reaction or trophic ulceration.

Discussion

A leprosy patient is defined as one who is found to have clinical signs and symptoms of the disease and who requires chemotherapy [1]. Paucibacillary leprosy (PBL) includes indeterminate (I), tuberculoid (TT), and borderline tuberculoid (BT) patients diagnosed clinically and histologically with the bacteriological index less than two on at any site [2].

Lesions of BT leprosy do not show well-defined margins, and the border of the lesion may be sloping outwards which may fade imperceptibly into the surrounding normal skin. Some cases may show extension of the primary lesion at one edge known as pseudopodium or small, discreet lesions surrounding the primary lesion known as satellite lesions. Skin lesions can differ in number (three to ten), size, and contour.

One of the important features of BT leprosy is the susceptibility to type 1 reactions in either skin lesions or nerves or both. Patients with long-standing BT leprosy often present to the OPD after the onset of type 1 reaction. Careful history taking and examination are necessary to elicit any nerve tenderness or early evidence of weakness or anesthesia of hands or feet requiring immediate intervention. If that's not the case, then BT leprosy may continue for many years with recurrent bouts of inflammation leading to progressive nerve damage, paralysis, and deformity.

In our case, the characteristic loss of sensations were absent, no peripheral nerves were enlarged, and also the number of lesions were uncharacteristic, which made the diagnostic journey of this case an interesting one. However, morphology of the lesion along with the histology confirmed the diagnosis of borderline tuberculoid leprosy. According to the spectrum of the disease, patient required paucibacillary regimen, but because of the presence of lepra bacilli in histopathology, patient was started on MB-MDT regimen along with supportive treatment, which again highlights the importance of skin biopsy in diagnosis and in defining the treatment regimen. Few other interesting cases have been reported in which clinically the lesions of leprosy mimicked angioedema, lupus vulgaris, cutaneous t-cell lymphoma, etc. [3] The uncommon disease presentations also include disease presenting with a single nodule or localized area of papules and nodules, Lucio leprosy, and spontaneous ulcerations seen in long-standing untreated lepromatous leprosy [4].

India is one of the countries where patients with paucibacillary leprosy constitute more than 70 percent of all leprosy patients [5]. The skin smear in BT leprosy is usually negative for AFB (L), or, at the most, only a few bacilli may be seen. Because of the low bacterial load, most of these patients are not infectious and are not considered to be important in spreading leprosy in the population. However, these patients constitute a large percentage of the total leprosy population who have a high rate of deformities [6]. By providing effective and appropriate treatment, the deformities and the associated morbidity can be easily prevented [7].

Sensory nerve supply of the face is mainly by **trigeminal nerve** (CN V), which provides sensory innervation via its ophthalmic division (CN V1), maxillary division (CN V2), and mandibular division (CN V3). The face has overlapping regions of sensory innervation which leads to the absence of characteristic lesional anesthesia in cases with tuberculoid spectrum of leprosy.

Leprosy is a spectral disease; its range of clinical presentations is wide. It can mimic many dermatological and neurological disorders. So, in an endemic country like India, we still need to have an eye to recognize the varied manifestations of leprosy, which emphasizes the importance of proper history and skin biopsy in diagnosing the challenging cases.

References

1. WHO. A guide to leprosy control. 2nd ed. Geneva: World Health Organization; 1988.
2. WHO. Chemotherapy of leprosy for control programme. Report of a WHO study Group. Tech Rep Ser 675. WHO; 1982.
3. Raval RC. Various faces of Hansen's disease. Indian J Lepr. 2012;84:155–60.
4. Jindal R, Shirazi N. Uncommon clinical presentations of leprosy: apropos of three case. Lepr Rev. 2016;87:246–51.
5. Rao PS, Subramanian M, Subramanian G. Parkash 1. Prospects for elimination of leprosy in India by 2000 AD. Indian J Lepr. 1995;67:285–92.
6. Rao PS, Subramanian M, Subramanian G. Deformity incidence in leprosy patients treated with multidrug therapy. Indian J Lepr. 1994;66:449–54.
7. WHO. Chemotherapy of leprosy. Report of a WHO Study Group. Tech Rep Ser 847. WHO; 1994.

Chapter 13
Annular Erythematous Plaque on the Right Hand

P. K. Ashwini

Abstract Leprosy is an infectious disease primarily involving the skin and peripheral nerves. Most important consequences of leprosy are due to nerve involvement. Neuritis is defined as inflammation of the nerves. The terms neuropathy and neuritis are used interchangeably. Neuritis is defined as pain in the neuro-anatomical area but in conjunction with motor impairment and/or sensory signs in the correspondent nerve, in addition to confirmed demyelinating signs demonstrated in the electrophysiological examination results. Neuropathic pain is defined as pain distribution in a neuro-anatomically plausible area with confirmed negative or positive sensory signs (i.e., hypoesthesia, hyperesthesia, hypoalgesia, hyperalgesia, or allodynia). Neural pain is a common complaint when a leprosy patient seeks medical consultation**.** Neuropathy in leprosy starts with the entry of *Mycobacterium leprae* into the Schwann cells of the small nerve fibers. Clinical examination focusing on the enlargement of peripheral nerves and also the triggered pain by nerve palpation are the clinical signs to predict neuritis. A detailed clinical examination is needed to identify the signs, which can otherwise be missed if the only presenting complaint of the patient is a vague neurological symptom. We hereby present a case who presented with such a trivial neurological symptom which on further clinical examination and evaluation revealed the presence of Hansen's disease. The relevance of clinical examination giving importance to signs is what is being highlighted.

Keywords Leprosy · Neuritis · Neuropathic pain

P. K. Ashwini (✉)
Department of Dermatology Venereology and Leprosy, JSS Medical College, JSSAHER, Mysuru, Karnataka, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_13

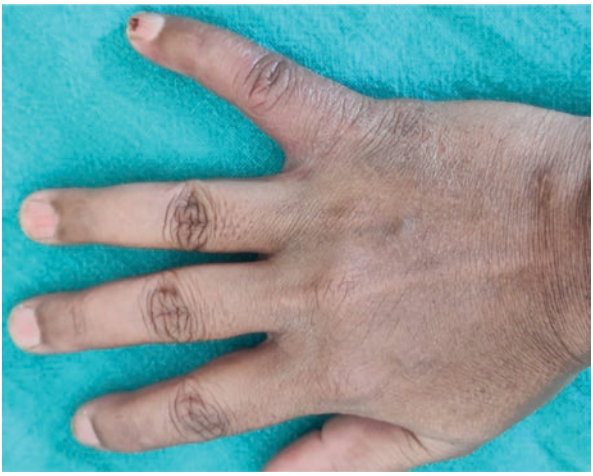

Fig. 13.1 Ill-defined dry erythematous patch over the right little finger extending into the fourth web space

Clinical Presentation

A 37-year-old female presented with a complaint of a vague dragging pain on the right-hand medial aspect for 4 months. She gave history of the low-grade pain, being present at the right elbow and radiating up to the little finger. She had noticed an asymptomatic reddish lesion on the right hand, to which various topical medications were prescribed earlier. There were no known medical comorbidities. On examination there was a solitary ill-defined dry erythematous patch over the right little finger extending into the fourth web space (Fig. 13.1). The patch had no sensory impairment. The right ulnar nerve was thickened and tender. No other peripheral nerve was thickened. Wartenberg's sign positivity was appreciated (Fig. 13.2). Systemic examination was normal.

What Is Your Diagnosis?

1. Resolving cellulitis.
2. Leprosy.
3. Dermatophytosis.

Investigation

- Slit skin smear was negative for acid fast bacilli.
- Skin histopathological examination revealed presence of multiple granulomas composed of epithelioid cells, lymphocytes, and Langhans giant cells around

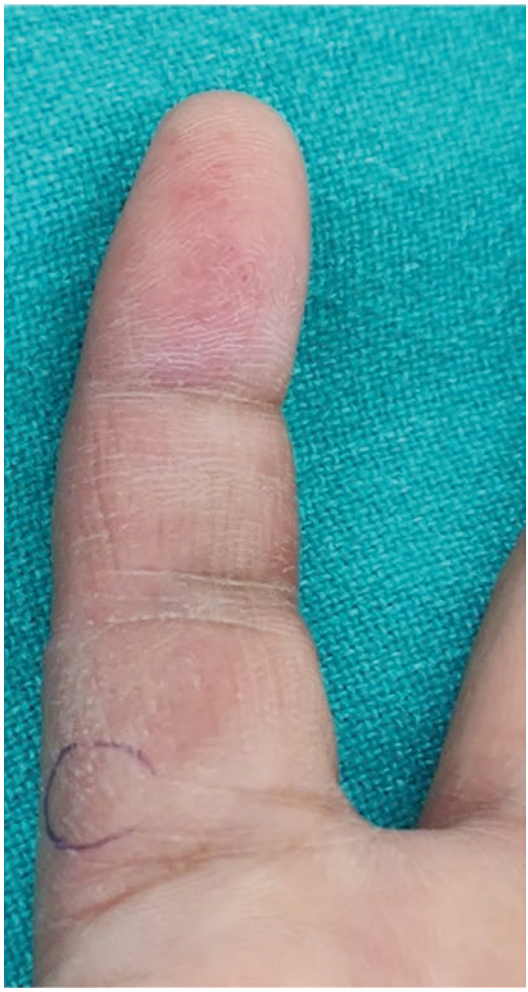

Fig. 13.2 Positive Wartenberg's sign

neurovascular bundles in the superficial and deep dermis. Fite-Faraco stain was negative for lepra bacilli. Features suggested borderline tuberculoid leprosy.

- Ultrasound of the thickened nerve using a 8 MHz probe revealed thickening of the right ulnar nerve 8 mm (Figs. 13.3 and 13.4) compared to the left ulnar nerve 2 mm (Fig. 13.5).
- Nerve conduction studies performed for both upper limbs affirmed abnormalities that were suggestive of sensorimotor axonopathy of the right ulnar nerve. Right ulnar nerve showed reduced compound muscle action potential and sensory nerve action potential amplitude with normal distal latency and conduction velocity.

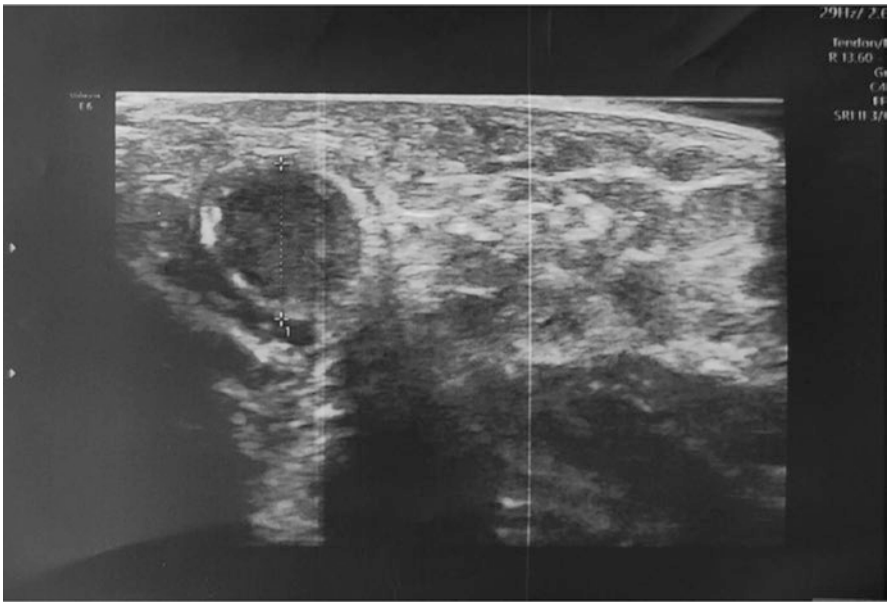

Fig. 13.3 High-resolution USG right ulnar nerve

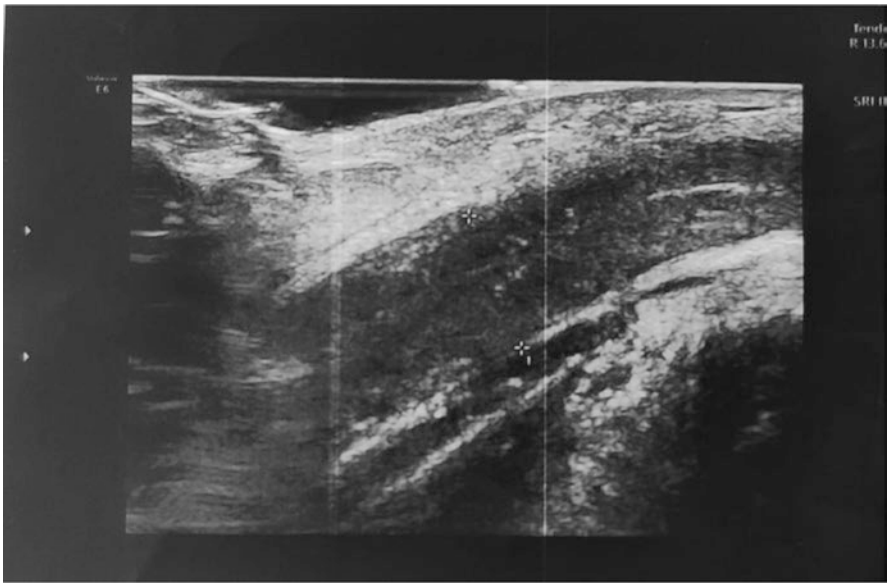

Fig. 13.4 High-resolution USG right ulnar nerve

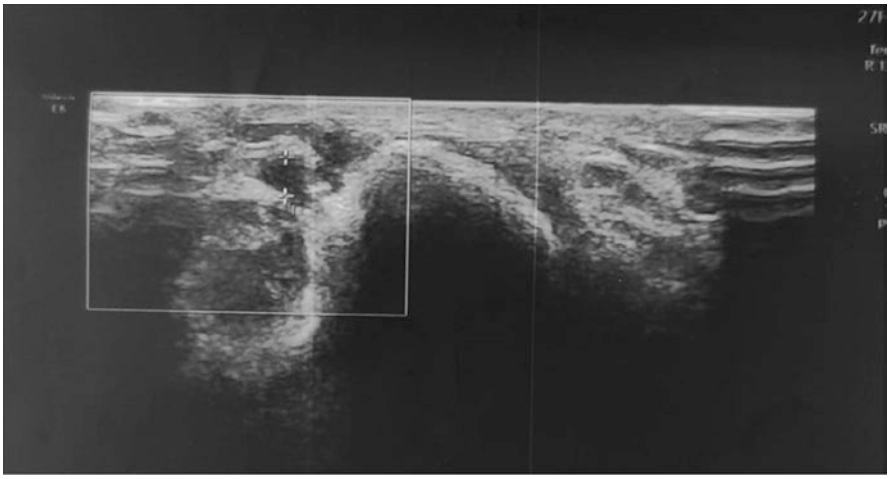

Fig. 13.5 High-resolution USG left ulnar nerve

Final Diagnosis

Borderline tuberculoid leprosy with type 1 reaction with right ulnar neuritis.

Discussion

The involvement of nerves is observed across the clinical spectrum of leprosy, and such cases are said to be having Hansen's neuritis (HN). HN can broadly be classified into four clinical types based on their period of occurrence and type of presentation. However, it should be noted that they are not mutually exclusive and can overlap one another:

1. Neuritis associated with the disease, which is usually chronic and low grade
2. Neuritis associated with reactions, which is usually acute and severe
3. Silent neuropathy or quiet nerve paralysis paralysis
4. Neuropathic pain in leprosy

Neuritis in leprosy is usually a subacute, demyelinating, and non-remitting event involving cutaneous nerves and larger peripheral nerve trunks. Invasion of Schwann cells and axons by *Mycobacterium leprae* leads to demyelination and axonal degeneration. Some of the most significant complications of leprosy occur as a result of the involvement of the peripheral nervous system [1].

One of the earliest nerves to be involved in Hansen's disease is the ulnar nerve. In case of ulnar palsy, the patient is unable to keep all the fingers straight and together, and the little finger tends to stay abducted from the ring finger and may

also be slightly bent or clawed. This is called Wartenberg's sign [5]. The muscle involved is the abductor digiti minimi.

Nerve involvement can be appreciated clinically in most cases. However, in some early cases, other modalities such as nerve ultrasound, nerve conduction studies, and nerve biopsies may be warranted.

The hallmarks of leprosy are nerve enlargement and inflammation. High-resolution ultrasonography (HRUS) can be used for imaging of nerves. Use of high resonance frequency (15–20 MHz) has made it very effective to visualize nerves. HRUS is efficient, user-friendly, and economical. Additional features such as compound imaging and panorama view make high-resolution ultrasonography a superior modality for imaging of nerves. High-resolution ultrasonography demonstrates nerve enlargement, even if subclinical. Inflammation can be detected by color Doppler study of involved nerves which show increased blood flow signals of endoneural and perineural vessels [6].

Nerve damage in leprosy may present as silent neuropathy without overt signs and symptoms or clinically manifest with weakness, atrophy, or contracture. Common methods used to detect sensory nerve function impairment are monofilament testing and ballpoint testing. For detection of motor function impairment, voluntary muscle testing is performed.

Functional derangement of nerves can be detected by nerve conduction studies before the appearance of clinical signs and symptoms. Disability and deformity could be minimized if nerve function impairment is detected and treated early. Nerve conduction studies involve the recording, display, measurement, and interpreting of action potentials arising from the peripheral nerves.

Nerve is stimulated through the skin with a surface stimulator or through a needle placed close to a nerve or a nerve root. Motor studies are performed by electrical stimulation of a nerve and recording the compound muscle action potential (CMAP) from surface electrodes overlying a muscle supplied by that nerve.

Conduction velocity (CV) is calculated by dividing the length of the nerve segment between the two stimulation points by the difference between the proximal and distal latency. Latency is the time from stimulus artifact to the onset of the response. The sensory nerve action potential (SNAP) is obtained by electrically stimulating sensory fibers and recording the nerve action potential at a point further along that nerve [7].

The electro-neuro-myographic pattern of leprosy neuropathy is described as the impairment of conduction of nerve impulse and decreased amplitude of sensory-motor potentials. Along with reduction in nerve conduction velocity, changes in latency are also reported. The slowing of sensory conduction velocity might show no difference between tuberculoid and lepromatous patients. In addition, a significant slowing of nerve conduction has also been reported in clinically normal nerves in leprosy. However, studies have reported the absence of correlation between neurological symptoms and electroneurographic studies in leprosy patients. A comprehensive electrophysiologic, ultrasonographic, and histological evaluation may be helpful in establishing a diagnosis of leprosy, where the presentation is more with neural symptoms.

In our case, multibacillary multidrug therapy (MB-MDT) was started. NSAIDs were given for neuritis. After 4 weeks of MB-MDT, she presented fever, fatigue, and reddish rashes over the body. On examination, there were erythematous maculopapular eruptions involving the face, trunk, and extremities. Drug hypersensitivity syndrome to dapsone was considered. Investigations confirmed the same with altered liver enzymes and eosinophilia. She improved with discontinuation of dapsone and injectable steroids. Patient was then started on ROM therapy and is being followed up.

Conclusion

Neurological symptoms commonly accompany cutaneous lesions in leprosy. Occasionally there can occur only neuritis at time of presentation without any overt clinical signs of cutaneous involvement. This may lead to significant delay in the diagnosis. Most deformities observed in leprosy are a consequence of delayed diagnosis of underlying nerve damage. The importance of prompt clinical and neurological examination is highlighted in the case.

References

1. Rao PN, Suneetha SK, Ebenezer GJ. Neuritis: definitions, clinicopathological manifestations and proforma to record nerve impairment in leprosy. In: Kumar B, Kumar HK, editors. IAL textbook of leprosy. 2nd ed. New Delhi Jaypee Brothers Medical Publishers; 2017. p. 400–1.
2. Naafs B, van Hees CL. Leprosy type 1 reaction (formerly reversal reaction). Clin Dermatol. 2016;34:37–50.
3. Haanpää M, Attal N, Backonja M, et al. NeuPSIG guidelines on neuropathic pain assessment. Pain. 2011;152(1):14–27.
4. Giesel LM, Hökerberg YH, Pitta IJ, et al. Clinical prediction rules for the diagnosis of neuritis in leprosy. BMC Infectious Diseases. 2021;21:1–9.
5. Sardana K, Khurana A. Jopling's handbook of leprosy, 6/E. CBS Publishers & Distributors Private Limited; 2021.
6. Rao P, Suneetha S. Pure neuritic leprosy: Current status and relevance. Indian J Dermatol Venereol Leprol. 2016;1:82.
7. Krishnan MI, Sobhanakumari K, Jose P, et al. High resolution ultrasound, nerve conduction study, and other non-invasive investigations in leprosy. J Skin Sex Transm Dis. 2021;16:1–7.

Chapter 14
A 50-Year-Old Male with Multiple Hypopigmented Macules and Patches

Rashmi Sarkar and Pooja Agarwal

Abstract Borderline lepromatous leprosy is one of the unstable variants of leprosy with a myriad of clinical cutaneous lesions. As most of the time, it occurs as a result of downgrading from an upper pole with numerous skin lesions, but not so well-defined and slightly infiltrated macules with coppery hue, round, or oval of about 2–3 cm in diameter are not so symmetrical. Infiltration takes place within the initial macules creating a plaque. The bacteriological index ranges from 3+ to 5+, and foamy macrophages along with lymphocytes characterize the histopathology. We presented a case of borderline lepromatous leprosy without any reaction and deformity.

Keywords Borderline leprosy · Numerous plaques · Asymmetrical · Foamy macrophage

Clinical Presentation

A 50-year-old male, resident of Uttar Pradesh, visited the dermatology OPD with hypoaesthetic hypopigmented skin lesions over both cheeks and forehead, bilateral upper limbs, upper back, chest, and both lower limbs for 1 year. For the past 3–4 months, the patient also complained of four episodes of fever, during which these lesions became more prominent. There was a complaint of tingling and numbness in the left leg for 3–4 months. There was no history of nasal stuffiness, epistaxis, testicular swelling, fall of objects from hands, or slippage of footwear. There was no history of any sharp shooting pain in limbs. On examination, there were numerous hypopigmented macules and patches distributed asymmetrically over the extremities, trunk, face, and buttock of size ranging from 5×6 cm^2 to 1×1 cm^2

R. Sarkar (✉)
Department of Skin & VD, Lady Hardinge Medical College, New Delhi, India

P. Agarwal
Department of Skin & VD, Smt. NHL Municipal Medical College, Ahmedabad, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_14

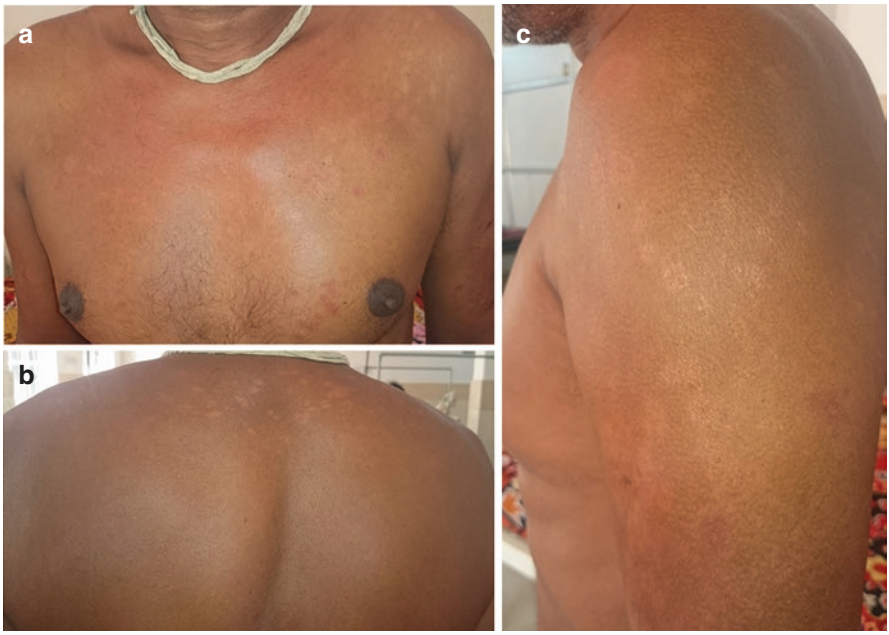

Fig. 14.1 (**a**) Multiple hypopigmented macule and patches over the chest. (**b**) Hypopigmented macules and patches over the upper back. (**c**) Hypopigmented macules and patches over the left arm

(Fig. 14.1a–c) There was a 20 to 30% loss of sensation over the patches. Both ulnar nerve enlargement (grade 1) and right posterior tibial nerve enlargement (grade 1) were present without tenderness. Other sensory, motor, and eye examinations were normal without any disability.

What Is Your Diagnosis?

- Borderline lepromatous leprosy
- Leishmaniasis
- Sarcoidosis
- Mycosis fungoides

Investigations

- Slit skin smear from the earlobe and lesion showed 3+ and 4+ BI, respectively.
- The skin biopsy taken from the smaller lesion showed epidermis atrophy, grenz zone, and granuloma consisting predominantly of macrophages with isolated

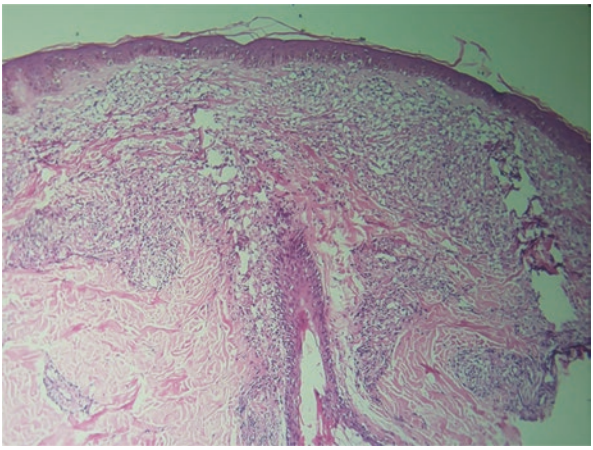

Fig. 14.2 Perineural infiltration consisting of lymphocytes, histiocytes, and foamy histiocytes (H&E ×100)

clumps of epithelioid cells. Macrophages show early foamy changes with intracellular bacilli frequently in spheroidal masses along with the absence of giant cells. Perineural infiltrates showed concentric infiltrate of lymphocytes, histiocytes, and foamy histiocytes giving a cut-onion appearance (Fig. 14.2).

- Serum ACE level was normal.
- Nerve USG: Uniform cylindrical thickening of bilateral ulnar, right common peroneal, and posterior tibial nerve.
- Nerve conduction study showed reduced amplitude of sensory and motor nerve action potential bilateral ulnar nerves.
- The Mitsuda reaction in the lepromin test was negative.

Final Diagnosis

Borderline lepromatous leprosy not in reaction with no disability

Discussion

Among five groups of Ridley-Jopling classification, tuberculoid (TT) and lepromatous leprosy (LL) are immunologically stable poles, while borderline tuberculoid leprosy (BT), borderline leprosy (BB), and borderline lepromatous (BL) are unstable types. These borderline types may up- or downgrade according to host cell-mediated immunity, and hence early detection and treatment are important to prevent disabilities and deformities.

Borderline lepromatous leprosy is characterized by numerous skin lesions which are distinct and are usually the result of downgrading from an upper pole, and it is

rare to find a de novo case of BL leprosy. The disease may begin with slightly infiltrated multiple small macules and papules having a coppery hue (not well appreciated in Indian skin tone) which are distributed over the body. The distribution of these macules does not follow any symmetrical pattern as is seen in lepromatous leprosy. It is not uncommon to find areas of apparently normal skin in between these lesions. As the disease progresses, papules, nodules, and plaques develop. When the disease has presented as a result of downgrading, the plaques may have bizarre geographical shapes and sloping margins which merge into the nearby normal skin. Along with the larger-sized plaques, multiple small papules may also be seen which indicate a further downgrading towards the lepromatous pole. The infiltration usually starts from the centre of the lesion and is more apparent in that part as compared to peripheral infiltration seen in borderline tuberculoid lesions. Facial and ear lobe infiltration may start appearing but is not as evident as in lepromatous leprosy, and the eyebrows are usually not or only partially affected.

Though there may be loss of sensation over the lesions along with a decrease in sweating and hair growth, it is less marked as compared to the BT leprosy lesions but more evident than LL leprosy lesions. The enlargement of peripheral nerves is usually asymmetrical as opposed to higher poles, and some patients may start developing glove and stocking type of anaesthesia also. BL patients are more prone to develop reactions because of the unstable nature of the disease. Type 2 reactions are more common than type 1 reactions, which occur only infrequently. Rare myriad presentations of borderline lepromatous leprosy which have been reported include psoriasiform and mycosis fungoides-like lesions, involvement of immune zones like palms, and lesions mimicking tinea versicolor [1–4].

Histopathological examination reveals an atrophic epidermis with a clear grenz zone separating the epidermis from the underlying macrophage granulomas. Some of the macrophages may have foamy cytoplasm. Leprosy bacilli are found in small globi and are plentiful. A small focus of epithelioid cells and occasional plasma cells may also be seen.

A characteristic feature is a dense clumped or widely scattered infiltrate of lymphocytes over the whole or a part of granuloma. It is of interest that lymphocytes are seen in only one another spectrum that is tuberculoid leprosy. Nerves are easy to identify with the peculiar, laminated appearance of the perineurium and perineural cell proliferation which has been likened to “onion skin.” A dense peripheral cuff of lymphocytes around a nerve bundle in a granuloma favours BL [5–7].

In our case, the diagnosis of borderline lepromatous leprosy was made by clinicohistopathological correlation, and we treated the patient with MB-MDT adult drug regimen for 2 years as the bacteriological index was more than 2+.

References

1. Gunawan H, Utami F, Achdiat PA, et al. A unique case of borderline lepromatous leprosy with psoriasis-like lesions all over the body and mycosis fungoides-like lesions on the face. J Clin Tuberc Other Mycobact Dis. 2019;17:100134.
2. Elwan NM, Neinaa YME. Borderline lepromatous leprosy: uncommon clinical presentation. Am J Dermatopathol. 2019;41:211–3.
3. Yang S, Makredes M, O'Donnell P, et al. A case of Hansen disease presenting as tinea versicolor. Dermatol Online J. 2013;19:7.
4. Day W, Prodanovic E. Borderline lepromatous leprosy masking as tinea versicolor. Int J Dermatol. 2019;58:125–6.
5. Job CK. Pathology of leprosy. In: Hastings RC, editor. Leprosy, vol. 12. 2nd ed. Edinburgh: Churchill Livingstone; 1994. p. 193–224.
6. Ridley DS. Classification. In: Ridley DS, editor. Pathogenesis of leprosy and related diseases, vol. 15. Butterworth and Co-Publishers Ltd; 1988. p. 155–75.
7. Jopling WH, McDougall AC. The disease. In: Handbook of leprosy. 5th ed. New Delhi: CBS Publishers and Distributors; 1996. p. 10–53.

Chapter 15
Multiple Asymptomatic Nodules on the Body

Swetalina Pradhan and Arpita Nibedita Rout

Abstract Leprosy is a chronic infectious disease with a wide spectrum of clinical manifestations. The lepromatous pole of the disease is characterised by the highest bacillary load and compromised cellular immunity. In this chapter, we have elaborated a clinical case scenario of lepromatous leprosy and have discussed the differential diagnoses, treatment approach and complications.

Keywords Lepromatous leprosy · Clinical manifestations

Clinical Presentation

A 36-year-old male, shopkeeper by occupation, presented with multiple asymptomatic skin-coloured nodules since 1 year. There was history of stuffiness of the nose on and off for 6 months. There was no history of leprosy or history of intake of anti-leprosy drugs in close contacts. On cross-questioning, there was a history of slipping of footwear on few occasions. There were no systemic symptoms. On examination, there were multiple discrete skin-coloured shiny nodules of size ranging from 0.2 to 0.3 cm over the face, ear lobules, trunk and extremities (Figs. 15.1 and 15.2). The surface was smooth for most of the nodules with only few showing central depression and crusting. The underlying skin was apparently normal. There was glove and stocking type of anaesthesia bilaterally, up to wrist and mid-calf level. Bilateral ulnar and common peroneal nerves were enlarged but non-tender, almost symmetrically. There was no clinically evident muscle weakness or visible deformity. All mucosal surfaces and palm soles were normal.

S. Pradhan
Department of Dermatology, AIIMS, Patna, Bihar, India

A. N. Rout (✉)
Department of Dermatology, AIIMS, Deoghar, Jharkhand, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_15

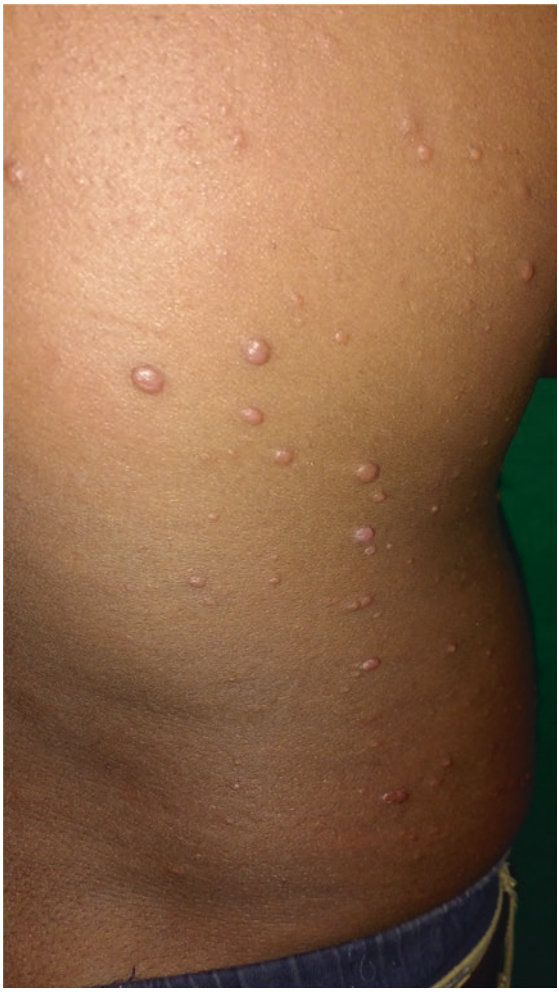

Fig. 15.1 Multiple skin-coloured discrete shiny nodules on the trunk

What Is Your Diagnosis?

1. Lepromatous leprosy
2. Multicentric reticulohistiocytosis
3. Sarcoidosis
4. Cryptococcosis

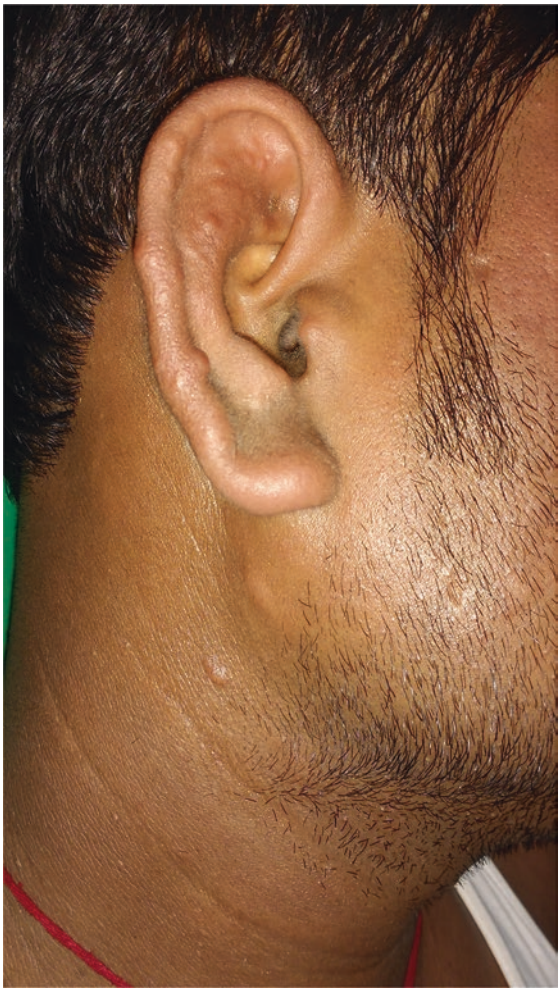

Fig. 15.2 Skin-coloured nodules on ear lobules

Investigations

All routine investigations such as complete blood count, liver and renal function tests, screening for HIV and hepatitis B and C virus were within normal limits. Nerve conduction study showed decreased sensory action potential and conduction velocity. Skin biopsy from the nodule on histopathological examination showed flattening of rete ridges, grenz zone and clusters of macrophages (Fig. 15.3). On modified Fite-Faraco stain showed plenty of intracellular bacilli in globi formation (Fig. 15.4).

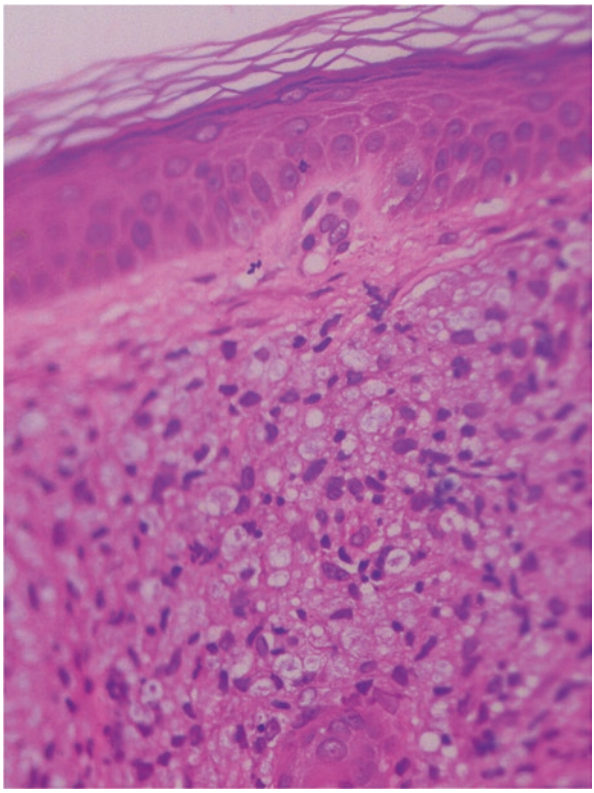

Fig. 15.3 Low power view showing epidermal atrophy, loss of rete ridges and collection of foamy macrophages in the dermis (H&E ×100)

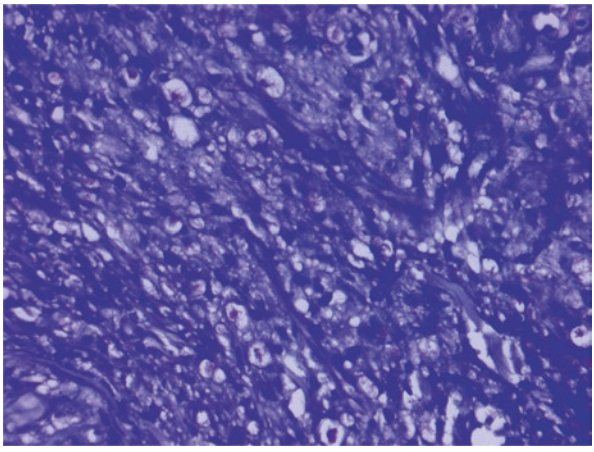

Fig. 15.4 Modified Fite-Faraco stain showing plenty of intracellular bacilli (×400)

Final Diagnosis: Lepromatous Leprosy

Lepromatous leprosy.

Discussion

Lepromatous leprosy is the most infectious type of leprosy with highest bacillary load and most compromised cellular immunity [1]. The proportion of cases of this group is showing an increasing trend gradually, as evident from the recent studies [2].

Clinically, lepromatous leprosy is characterised by varied manifestations such as diffuse infiltration of the skin, skin-coloured shiny nodules or shiny maculopapular lesions over the ear lobules, trunk, extremities or unusually over mucosal surfaces, numerous and distributed symmetrically. The involvement of peripheral nerves is usually symmetrical, slightly enlarged or apparently of normal thickness but can be asymmetrical or associated with nodularity or fusiform enlargements if the disease has downgraded from the tuberculoid pole. There may be distal sensory and autonomic neuropathy, which is described as glove and stocking type of anaesthesia and is often bilaterally symmetrical [3].

There may be involvement of various systems which may be apparent clinically, or there may be laboratory abnormalities. There may be nasal stuffiness, epistaxis, resorption of nasal and distal phalangeal cartilage and bone, loss of eyebrows and eyelashes, corneal dryness and ulceration, abnormalities of renal and hepatic parameters, anaemia, gynaecomastia or testicular atrophy [4].

The diagnosis is often clinical. Investigations, mostly slit skin smear, histopathology and liver and renal function tests, are required to exclude the differentials and to rule out systemic involvement. In histopathological examination, there is epidermal atrophy, flattening of rete ridges, sub-epidermal grenz zone and sheets of macrophages in the upper dermis. Modified Fite-Faraco stain is used to demonstrate the intracellular organisms. Slit skin smear from the skin nodules on Ziehl-Neelsen stain shows plenty of acid-fast bacilli either lying singly or in globi formation. Nerve conduction study shows the sensory and motor nerve function abnormality [5].

The skin nodules of lepromatous leprosy can be confused with nodules of xanthomatosis, sarcoidosis, multicentric reticulohistiocytosis and post-kala-azar dermal leishmaniasis. Associated features such as sensory loss, nerve enlargement and other systemic features if present can point towards the diagnosis.

Disease course is complicated by inflammatory episodes of type 2 lepra reaction and erythema nodosum leprosum. There can be long-term complications which may persist even after treatment completion such as claw hand, foot drop, resorption of digit, lagophthalmos, ectropion, trichiasis, corneal opacity and ulceration, acute or chronic iritis, synechiae, gynaecomastia, testicular atrophy and residual anaesthesia, leading to episodes of trophic ulcers, infections and osteomyelitis.

Various complications related to treatment include acquired ichthyosis, brownish pigmentation and complications of long-term steroid use.

Multidrug therapy with rifampicin, clofazimine and dapsone for 12 months is the standard treatment recommendation, in the absence of lepra reactions. Counselling for adherence to therapy and care of anaesthetic areas is also important.

The present case was diagnosed as lepromatous leprosy based on the suggestive pointers in history such as stuffiness of the nose, slippage of footwear and typical clinical features such as asymptomatic skin-coloured shiny nodules with glove and stocking-type anaesthesia and symmetrical enlargement of peripheral nerves. Histopathological findings of intracellular bacilli confirmed the diagnosis. The patient was started on multidrug therapy treatment as per WHO recommendation. There were no associated complications.

References

1. Dorilêo GB, Cavalcante LRDS, Lopes JC, Damazo AS. Report of two cases of lepromatous leprosy at an early age. Int J Infect Dis. 2020;101:46–8. https://doi.org/10.1016/j.ijid.2020.09.1448. Epub 2020 Sep 28.
2. Mushtaq S, Dogra N, Dogra D, Faizi N. Trends and patterns of leprosy over a decade in a tertiary care hospital in northern India: a retrospective analysis. Indian J Dermatol Venereol Leprol. 2020;86:141–9.
3. Kumar B, Dogra S. Case definition and clinical types of leprosy. In: Kumar B, Kar HK, editors. IAL textbook of leprosy. 2nd ed. India: Jaypee Brothers medical Publishers; 2017. p. 236–53.
4. Panda JK, Nayak M, Rout AN, Jena S. Systemic manifestation of leprosy: a comprehensive epidemiological study from eastern India. J Med Sci Clin Res. 2017;5:22626–34.
5. Ponnaiya J. Laboratory diagnosis. In: Kumar B, Kar HK, editors. IAL textbook of leprosy. 2nd ed. India: Jaypee Brothers Medical Publishers; 2017. p. 278–89.

Chapter 16
Skin-Coloured Nodules and Atrophic Scars

Abhishek Bhardwaj and M. Bandhala Rajan

Abstract Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. The causative agent is unique in that it cannot be grown in artificial media, till date. The disease is represented by a continuum of varied clinical features with two polar forms, the 'paucibacillary' tuberculoid leprosy and 'multibacillary' lepromatous leprosy. The clinical features are more or less limited to the skin, peripheral nervous system, upper respiratory tract, eyes, bones and testes. The onset of the disease on the lepromatous pole is subtle, and unless noticed with a keen eye, the diagnosis is generally delayed. The disease is still stigmatized, although most cases respond well to WHO-mandated multidrug therapy. With the lowering of the number of cases, it is imperative that clinicians should observe the indolent disease and keep it in the back of their minds especially in endemic areas.

Keywords Lepromatous leprosy · *Mycobacterium leprae* · Mimic

Clinical Presentation

A 58-year-old male presented with a 10-year history of numbness over bilateral hands and feet with multiple skin-coloured nodules over the trunk and extremities. In the past, the patient also had multiple episodes of intermittent fever with recurrent painful nodules over extremities. These nodules ulcerated to discharge pus and healed within 5–7 days leaving behind atrophic scars. Patient received some

A. Bhardwaj (✉)
Department of Dermatology, Venereology & Leprology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

M. Bandhala Rajan
Department of Dermatology, Venereology & Leprology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

Department of Dermatology, Venereology & Leprosy, Trichy SRM Medical College and Research Centre, Tiruchirapalli, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_16

undocumented oral medications, following which patient didn't develop any painful eruptions further in the past 1 year; however, skin-coloured nodules and numbness persisted. Patient was a known diabetic on oral hypoglycaemic drugs for 4 years. Patient was afebrile during examination, and significant lymphadenopathy (1.5 cm × 1 cm to 2.5 cm × 2 cm) was noted over left cervical (level III), bilateral axillary and inguinal regions. Mucocutaneous examination revealed diffuse infiltration of the skin over back and bilateral thighs, multiple skin-coloured firm nodular lesions over the trunk and bilateral extremities with multiple hyperpigmented atrophic scars over bilateral extremities (Fig. 16.1a–d). Gynecomastia was also observed. Peripheral nerve examination revealed non-tender, symmetrical grade III

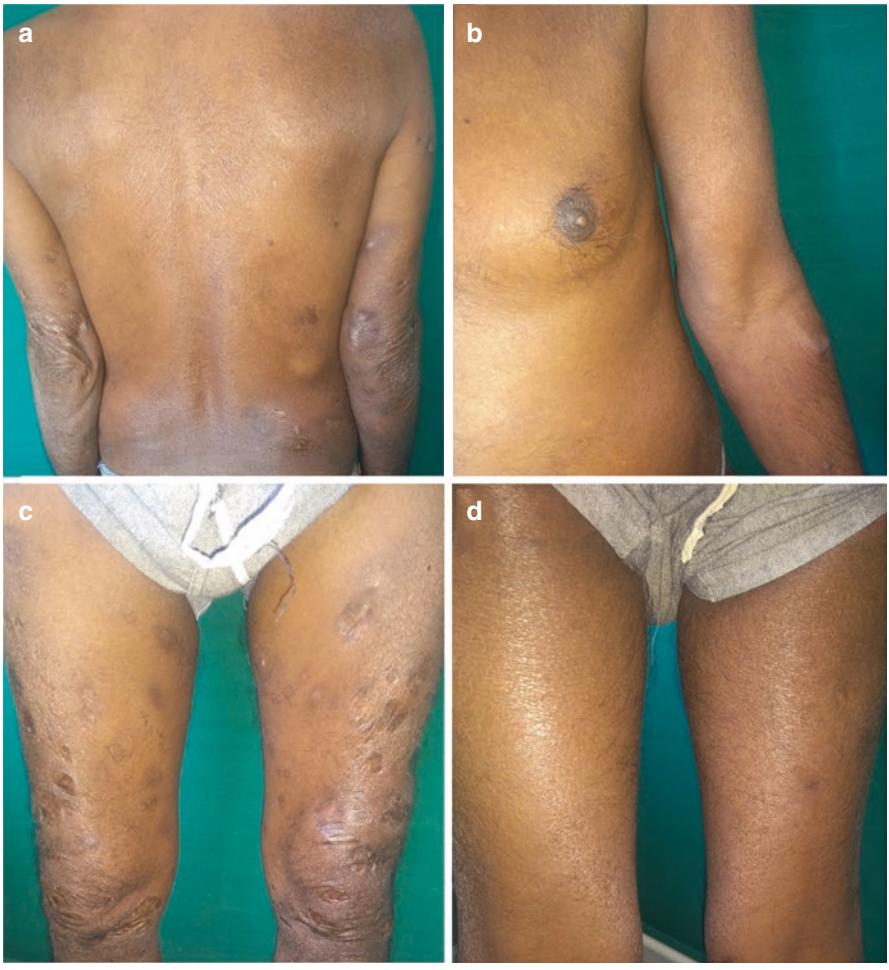

Fig. 16.1 Clinical images. (**a**) Image showing ill-defined infiltration of the skin over the upper and lower back and multiple hyperpigmented nodules and atrophic scars over the arms and elbows. (**b**) Image showing gynecomastia and single skin-coloured nodule over the left forearm. (**c**) Image showing ill-defined hyperpigmented patches with multiple atrophic scars over bilateral anterolateral thighs. (**d**) Image showing infiltrated shiny skin over posterior aspect of bilateral thighs

thickening of bilateral ulnar, radial cutaneous, lateral popliteal and posterior tibial nerves. Sensory examination revealed glove and stocking pattern of anaesthesia with patchy loss of temperature and pain sensation over bilateral legs. Motor examination didn't reveal any muscle weakness.

What Is Your Diagnosis?

1. Lepromatous leprosy
2. Borderline lepromatous leprosy
3. Poorly controlled type II diabetes mellitus with recurrent furunculosis
4. Papulonecrotic tuberculid

Investigation

- Baseline haematological investigations were unremarkable except moderate anaemia (Hb-10 g/dL).
- Slit skin smear from four sites (bilateral ear lobes and eyebrows) showed multiple acid-fast bacilli with an average bacteriological index of 5.25 with 20% live intact bacilli.
- Histopathology of skin-coloured nodules revealed focal thinning of the epidermis with sub-epidermal grenz zone. Superficial and deep dermis showed multiple foamy histiocytes and few epithelioid histiocytes, and Fite-Faraco stain showed numerous lepra bacilli (Fig. 16.2a, b).
- Right radial cutaneous nerve biopsy and left cervical lymph node biopsy also showed similar infiltrate of foamy histiocytes with Fite-Faraco showing numerous acid-fast bacilli.

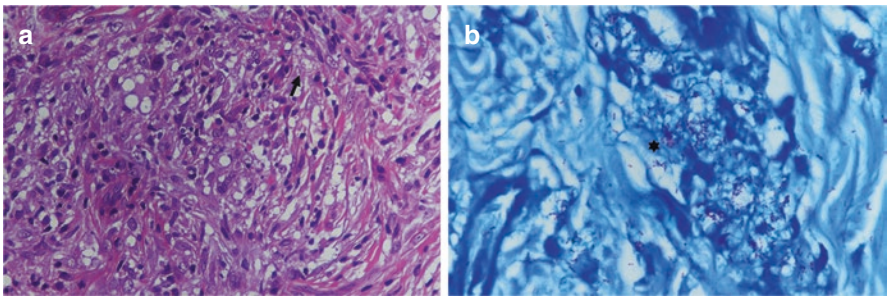

Fig. 16.2 Histopathological images. (Courtesy Dr. Poonam Elhence). (**a**) Section shows superficial and mid-dermis with elongated histiocytic cells and several foamy histiocytes (black arrow) with debris and negative shadows in the cytoplasm (400×, H&E). (**b**) Section shows several scattered and few clumps of beaded acid-fast positive bacilli (asterix) in the foamy histiocytes in the superficial dermis and mid-dermis (1000×, Fite-Faraco stain)

- Nerve conduction study revealed distal symmetrical small and large fibre, predominantly sensory polyneuropathy involving bilateral lower limbs.

Final Diagnosis

Polar lepromatous leprosy (LL) with WHO grade 1 disability.

Discussion

Leprosy has been traditionally acknowledged as a mimic. It has myriad presentations, behaving more like a continuum than a single expression of disease. Lepromatous leprosy (LL) is a multibacillary form of leprosy with the weakest cell-mediated immunity against the bacillus. An important distinction that needs to be acknowledged regarding LL is that it can be described qualitatively to be of two types: LLp, the rare polar form which arises de novo and is immunologically stable, and LLs, the commoner subpolar type which results from natural downgrading in patients with poor T-cell-mediated immunity. The polar variant is a public health challenge because symptoms are minimal and the patient harbours millions of bacilli. Such cases are potentially infectious [1].

The cutaneous manifestations of leprosy depend on the spectrum in which the patient is identified at the time of diagnosis. Skin findings of the tuberculoid end of the spectrum can be striking, but they gradually become subtle towards the lepromatous spectrum (LL). The lesions can be numerous, uncountable in LL. There can be diffuse infiltration of the skin or skin-coloured to faintly erythematous nodular lesions with no surface dryness or loss of hair. The loss of sensation over the lesions is minimal. Only in advanced cases, the classical gloves and stocking anaesthesia can be elicited [1].

Characteristic feature of LL is the infiltration of the skin over the central face with increased skin folds and loss of eyebrows and eyelashes, termed “leonine facies” or lion-like face. Nasal mucosa is commonly involved in LL, leading to crusting, epistaxis and damage of the nasal septum causing “saddle nose”. Palatal perforation is also noted in untreated LL cases. With the advent of multidrug therapy, such florid findings are increasingly becoming rarer [2]. Other nonspecific cutaneous findings are gynecomastia, bilateral pedal oedema and ichthyosis of the skin [1].

There are various complications noted in LL patients. The subtle anaesthesia predisposes these patients to develop unexplained blisters or ulcers over extremities. Often patients are unable to recall the reason of such sudden changes. On detailed history taking with direct questions, some of them may remember proximity to fire, e.g. during cooking. It is pertinent to point out that in patients who smoke tobacco (bidis or cigarettes), one can find either small burns or scars of previous burns

around fingers which the patient uses to hold the cigarette. In manual labourers, trophic ulcers over the pressure bearing areas of the sole, too, are common. An extra effort should be made to look at the feet of the patient diligently. On examination, active ulcers on the dorsum of the feet, clawing of the toes, calluses, trophic ulcers and in advanced cases the collapse of plantar arches may be noted. Another complication to be mindful of is that 60% cases of LL suffer from type 2 lepra reaction. This reactional state may be the presenting feature at the time of diagnosis [3].

Eyes are another area which must be examined in each case of leprosy especially LL. Eyes can get affected in leprosy, due to direct infiltration, cranial nerve involvement or inflammation and reactions. Among all leprosy, the lepromatous variant affects the patient systemically causing musculoskeletal changes, testicular atrophy (soft consistency on palpation, gynaecomastia due to inadequate testosterone production), renal involvement, reticuloendothelial system involvement, adrenal insufficiency, autonomic nervous system dysregulation and haematological changes underlining that LL needs to be seen as a systemic illness [1].

Although cutaneous findings such as diffuse infiltration and nodular lesions are more common in lepromatous leprosy (LL), these can occasionally be seen in borderline lepromatous cases too [4]. In such clinical conundrums, it will be worthwhile to note that symmetries of cutaneous lesions as well as neural involvement are important clues pointing towards lepromatous leprosy (Table 16.1) [5]. The following conditions can also be considered as occasional differentials for polar LL: erythema elevatum diutinum, juvenile xanthogranuloma, steatocystoma multiplex, trichoepithelioma, cutaneous leishmaniasis, keloidal blastomycosis, cutaneous tuberculosis, blastomycosis, chromoblastomycosis, post-kala-azar dermal leishmaniasis (PKDL) and sarcoidosis [6]. The differentials can vary not only from case

Table 16.1 Differences between BL and LL [5]

S. No	Characteristics	Borderline lepromatous leprosy	Lepromatous leprosy
1.	Number of lesions	>30	Innumerable
2.	Distribution of lesions	Asymmetrical distribution but tendency towards symmetry	Symmetrical distribution
3.	Peripheral nerve thickening	Multiple, asymmetrical	Multiple, bilaterally symmetrical thickening
4.	Sensory loss	Slightly diminished over lesions Glove and stocking anaesthesia is not common	Minimally diminished/no sensory loss over lesions Glove and stocking anaesthesia present
5.	Reactions	More common Both type 1 and type 2 reactions can occur	Less common Only type 2 reactions can occur
6.	Bacteriological index	3 to 4+	5 to 6+, globi
7.	Histopathology	No clear-cut grenz zone Granuloma contains foamy macrophages and few epithelioid cells	Well-defined grenz zone present Granuloma contains only foamy macrophages

to case but also from region to region. For example, cutaneous leishmaniasis can be a differential in a case with limited nodules in dry areas of Western India, while post-kala-azar dermal leishmaniasis (PKDL) becomes an important differential in endemic Eastern parts of the subcontinent [6].

Slit skin smear and histopathological examinations are traditional tools to confirm the spectrum of leprosy. Slit skin smear of lepromatous leprosy shows high bacteriological index (5+ or 6+), and histopathology shows atrophic epidermis and sub-epidermal grenz zone with superficial and deep dermal infiltration of foamy histiocytes [1, 2]. With time dermoscopy, PCR-based assays, high-resolution ultrasonography of peripheral nerves, ELISA and lateral flow assays too have added into the armamentarium of investigations. These newer investigations are recent advances with varied sensitivity and specificity and therefore are still not part of WHO guidelines for diagnosis of leprosy [7].

Although our case was a histopathologically confirmed case of LL, there were some atypical findings such as lymphadenopathy, which made our case interesting. Lymph node infiltration by leprosy bacilli is rarely reported in literature [8].

Treatment of lepromatous leprosy is by multidrug therapy composed of daily dapsone (100 mg) and clofazimine (50 mg) with monthly once rifampicin (600 mg) and clofazimine (300 mg). The duration of treatment as per WHO is 12 months. However, some authors suggest an additional 12–36 months of MDT or till smear negativity in multibacillary patients (BI > 4+) [9]. Studies also showed that addition of immunotherapy with bacillus Calmette-Guérin (BCG) or *Mycobacterium welchii* vaccine may help to reduce the duration of treatment by 50% [10].

Early diagnosis, adequate treatment and long-term follow-up are key in the management of LL to reduce the infectivity and to prevent progression of disabilities.

References

1. Sardana K, Khurana A. Handbook of leprosy. CBS Publishers & Distributors; 2020.
2. Fischer M. Leprosy—an overview of clinical features, diagnosis, and treatment: CME article. JDDG J Dtsch Dermatol Ges. 2017;15(8):801–27.
3. Salvi S, Chopra A. Leprosy in a rheumatology setting: a challenging mimic to expose. Clin Rheumatol. 2013;32(10):1557–63.
4. Shelley BP, Shenoy MM. Revisiting Hansen's disease: recognizing the many neurodermatologic faces and its diagnostic challenges. Arch Med Health Sci. 2018;6(1):157.
5. Kumar B, Dogra S. Case definition and clinical types of leprosy. In: Kumar B, Kar HK, editors. IAL textbook of leprosy. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2017. p. 244–7.
6. Maymone MBC. Leprosy: clinical aspects and diagnostic techniques. J Am Acad Dermatol. 2020;83(1):14.
7. 9789290226383-eng.pdf. https://apps.who.int/iris/bitstream/handle/10665/274127/9789290226383-eng.pdf.
8. Gupta S, Mehta A, Lakhtakia R, Nema SK. An unusual presentation of lepromatous leprosy. Med J Armed Forces India. 2006;62(4):392–3.
9. Malathi M, Thappa DM. Fixed-duration therapy in leprosy: limitations and opportunities. Indian J Dermatol. 2013;58(2):93–100. https://doi.org/10.4103/0019-5154.108029.
10. Sehgal VN, Sardana K. Immunoprophylaxis of leprosy: current status and future prospects. Indian J Dermatol Venereol Leprol. 2007;73:71–2.

Chapter 17
70-Year-Old Male with Nodules over Frictional Areas

Vikas Shankar and Rashid Shahid

Abstract Lepromatous leprosy usually presents as symmetrically distributed, small, multiple, shiny hypopigmented, erythematous, or coppery, shiny macules, papules, and nodules with normal sensation or mild sensory loss. The infiltration of the skin of the face with loss of eyebrows, eyelashes, and nasal septum destruction gives the appearance of leonine facies. The nerve involvement is symmetrical with glove and stocking anesthesia. The lepromin test is negative. In the following chapter, a clinical case scenario of lepromatous leprosy has been elaborated who has nodular lesions which mimicked xanthomas clinically.

Keywords Lepromatous leprosy · Leonine facies · Globi · Xanthoma

Clinical Presentation

A 70-year-old male patient, farmer by occupation, resident of Bihar presented in our outpatient department with multiple and asymptomatic skin-colored to yellowish nodular eruptions over extremities and trunk for the last 1 year. There was no history of similar problems in family members. The patient gave history of intermittent epistaxis. Also, there was no history of hyperlipidemia and cardiovascular disease among family members. Physical examination showed multiple discrete skin-colored to yellowish shiny nodular eruptions over the bilateral knees, elbows, trunk, Achilles tendons, dorsum of the hands, palms, soles, and scrotum of size ranging from 0.2 to 0.6 cm in diameter predominantly in frictional areas (Figs. 17.1, 17.2, 17.3, 17.4). Sensory examination revealed patchy loss of sensation over bilateral upper and lower extremities. Non-tender, bilaterally symmetrical thickening of the ulnar and common peroneal nerve was present.

V. Shankar (✉)
Department of Dermatology, PMCH, Patna, Bihar, India

R. Shahid
Department of Dermatology, AIIMS, Patna, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_17

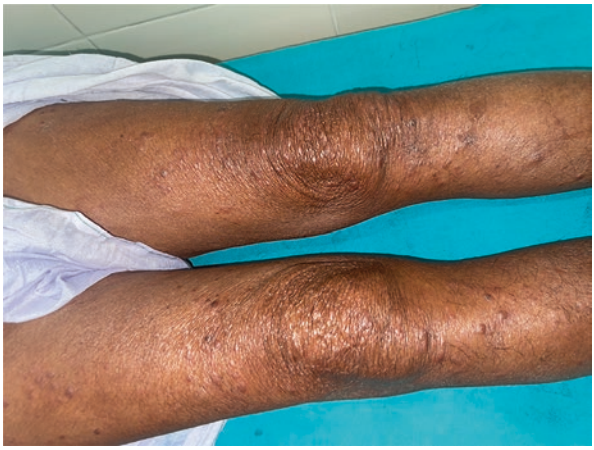

Fig. 17.1 Multiple nodules over bilateral knees

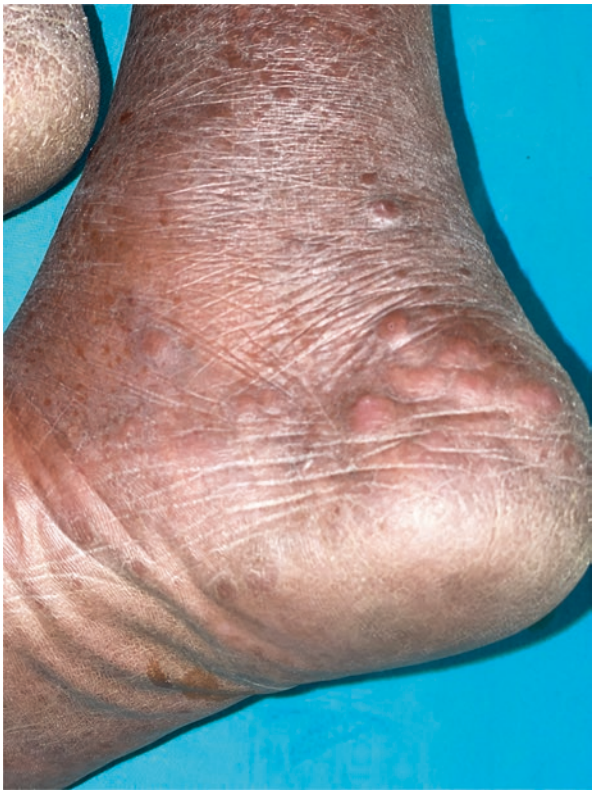

Fig. 17.2 Skin-colored to yellowish nodules over the Achilles tendon

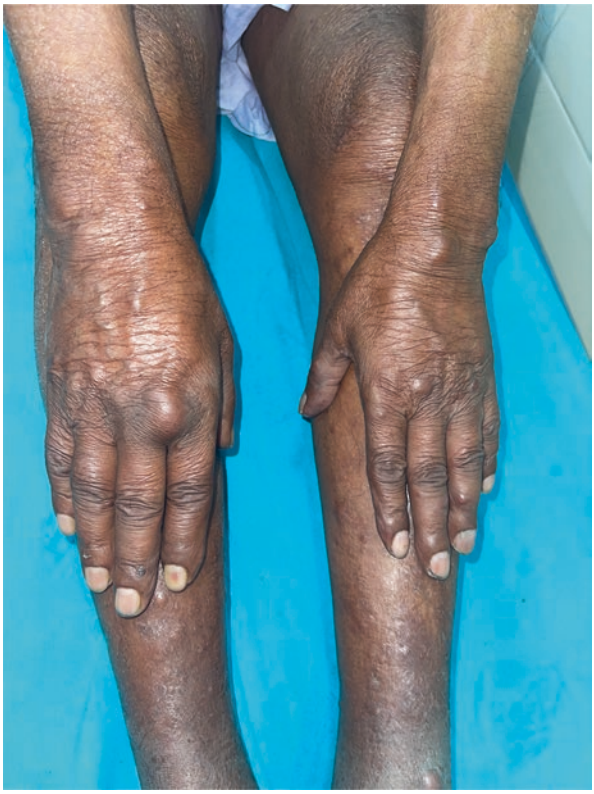

Fig. 17.3 Nodules over the dorsum of the hand

What Is Your Diagnosis?

- Lepromatous leprosy
- Xanthoma
- Sarcoidosis
- Leishmaniasis

Investigation

- Routine hematological parameters revealed mild anemia with Hb 11 gm%; serum ACE and fasting lipid profile were normal.
- Slit skin smear from the eyebrows, earlobes, and the lesional areas showed many acid-fast bacilli (BI = 3+).
- Skin biopsy from the shiny skin-colored nodule showed epidermal atrophy with a grenz zone. There were multiple foamy histiocytes and few lymphocytes located around perivascular, periappendegeal, and perineural. Multiple acid-fast bacilli arranged in globi are present (Fig. 17.5). No sub-epidermal edema or neutrophile is seen in the infiltrate.
- USG of nerve showed symmetrical nerve thickening of the ulnar nerve, radial cutaneous nerve, and common peroneal nerve.

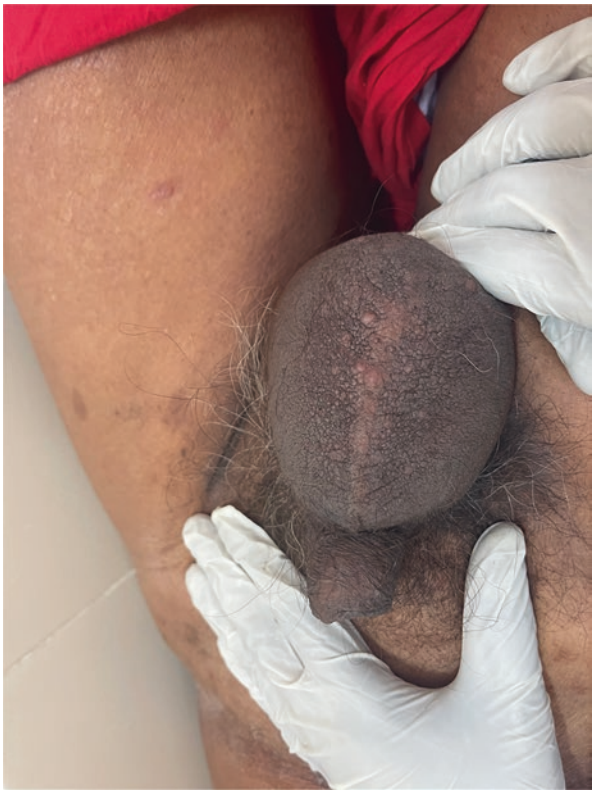

Fig. 17.4 Nodules over the scrotum

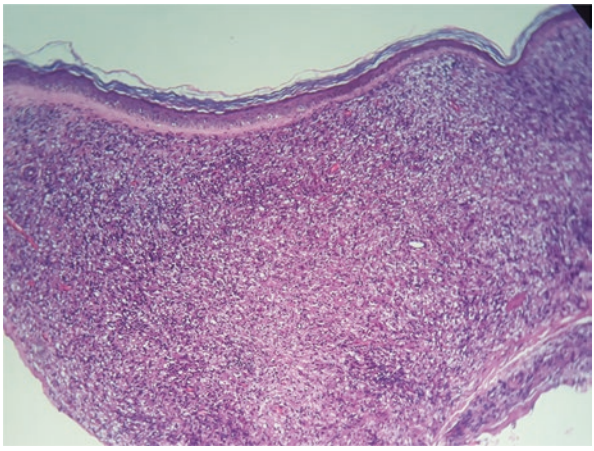

Fig. 17.5 Foamy macrophages throughout the dermis (H&E ×100)

Final Diagnosis

Lepromatous leprosy not in reaction without disability.

Discussion

Lepromatous leprosy patients have low cellular immunity and high bacillary load [1]. The proportion of lepromatous leprosy cases is on an increasing trend [2]. The morphological presentations include macules, papules, nodules, and plaques which are usually widespread, symmetrical in distribution. The most common sites involved are the face, ear lobules, trunk, extremities especially over joints, elbows, fingers, buttocks, genitalia, and rarely mucous membranes also. Delayed treatment can lead to diffuse infiltration by bacilli in body parts resulting in thickening of the skin in the ear (Buddha ear) and face (leonine facies). Systemic involvement included epistaxis, blocked or stuffy nose, corneal xerosis, ulceration, lagophthalmos, bony resorption, gynecomastia, anemia, and atrophy of testis. Bilaterally symmetrical gloves or stocking anesthesia may be present [3]. Edema over bilateral ankles and legs is found due to increased capillaries permeability and gravity [4].

The diagnosis of lepromatous leprosy is often based on clinical features. However, in some cases of diagnostic dilemma investigations like skin biopsy, slit skin smear, and nerve conduction, study should be done. Histopathological findings of lepromatous leprosy include atrophy of the epidermis, rete ridges flattening, subepidermal grenz zone, and macrophages in the upper dermis. Slit skin smear shows plenty of acid-fast bacilli with Ziehl-Neelsen stain. Nerve conduction study shows abnormality of sensory and motor nerve function. Cases of lepromatous leprosy without lepra reaction are treated with WHO treatment guidelines: rifampicin, clofazimine, and dapsone for 12 months. Patients are counseled to complete their treatment and care of anesthetic areas (Fig. 17.6).

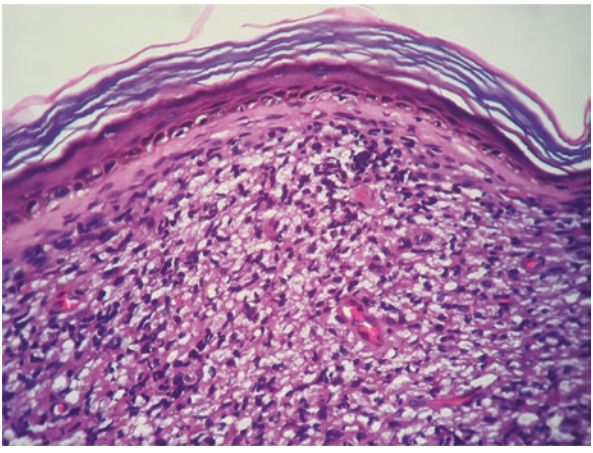

Fig. 17.6 Grenz zone, foamy macrophages, and scant lymphocytes (H&E ×400)

Current case presented with skin-colored to yellowish nodules predominantly over frictional areas mimicking xanthoma lesions and was later on diagnosed as lepromatous leprosy based on clinicohistopathological correlation. The patient was started on multiple drug therapy as recommended by WHO for 24 months because of a high bacteriological index.

References

1. Dorilêo GB, Cavalcante LRDS, Lopes JC, Damazo AS. Report of two cases of lepromatous leprosy at an early age. Int J Infect Dis. 2020;101:46–8.
2. Mushtaq S, Dogra N, Dogra D, Faizi N. Trends and patterns of leprosy over a decade in a tertiary care hospital in northern India: a retrospective analysis. Indian J Dermatol Venereol Leprol. 2020;86:141–9.
3. Panda JK, Nayak M, Rout AN, Jena S. Systemic manifestation of leprosy: a comprehensive epidemiological study from eastern India. J Med Sci Clin Res. 2017;5:26–34.
4. McDougall AC, Archibald GC. Lepromatous leprosy presenting with swelling of legs. Br Med J. 1977;1:23–4.

Chapter 18
A-30-Year-Old Male with Left Foot Drop

Dependra Kumar Timshina

Abstract Leprosy is primarily a disease of the peripheral nerves. Diagnosis of leprosy in absence of dermatological manifestations is challenging. Nerve involvement in leprosy begins early in the disease and, sometimes, can be the only manifestation. Though leprosy is a treatable disease, nerve involvement can lead to significant deformity, disability, and stigma. It can mimic other neuropathies like diabetes mellitus, etc. Pure neuritic leprosy most of the times remains undiagnosed due to absence of skin lesions which later on leads to deformity because of progressive nerve damage. We are discussing a case of pure neuritic leprosy who presented with foot drop.

Keywords Pure neuritic leprosy · Acid-fast bacilli · *Mycobacterium leprae* Neuritis · Nerve abscess

Clinical Presentation

A 30-year-old male, driver by occupation, presented with complaints of pain and weakness of the left leg along with difficulty lifting his left foot off the ground for 1 month. He gave a history of difficulty in squatting for the past 3 months. The patient had a history of tingling and burning for 1 year for which he was treated with multivitamins. Gradually the condition worsened, and he presented with weakness of his left leg. Bowel and bladder habits were normal. On clinical examination, there was decreased sensation below the knee, along the distribution of the common peroneal nerve. Grossly thickened and mild tender, a lobulated common peroneal nerve was felt. The patient was not able to dorsiflex the left foot. Left tibialis anterior, extensor hallucis longus, and extensor digitorum longus muscles had the power of 2/5. There was no patch over the skin or any loss of hair.

D. K. Timshina (✉)
Remedy Clinics, Siliguri, West Bengal, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_18

What Is Your Diagnosis?

- Pure neuritic leprosy (PNL) with grade 2 disability.
- Diseases that produce thickening of the peripheral nerves (Dejerine-Sottas hypertrophic neuritis and von Recklinghausen disease).
- Diseases producing atrophy of leg muscles (polyneuritis, poliomyelitis).
- Systemic diseases producing mononeuritis (paraneoplastic and Bernhardt and Roth's meralgia paresthetica).

Investigations

- Ultrasonography of the nerve showed thickened nerve with diffuse and focal hypo-and hyperechoic foci indicating nerve abscess suggestive of thickened nerve with abscess.
- Fine needle aspiration cytology of the nerve abscess under ultrasound guidance showed the presence of acid-fast bacilli (AFB) (Fig. 18.1).
- Slit skin smear- no acid-fast bacilli found.

Final Diagnosis

Pure neuritic leprosy without reaction with grade 2 disability.

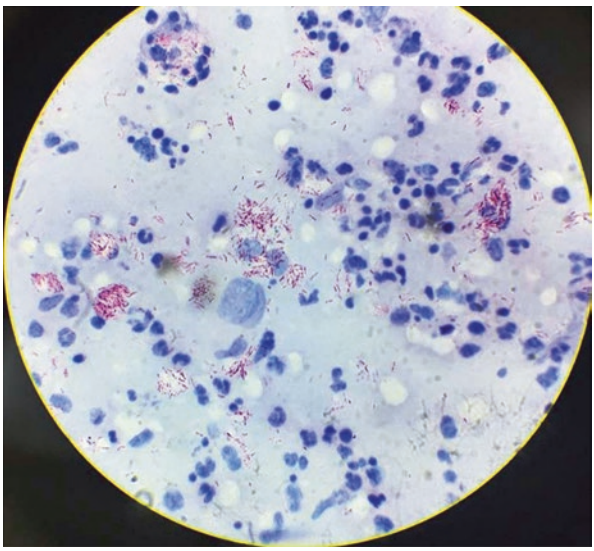

Fig. 18.1 AFB stain of the FNAC of the nerve showing acid-fast bacilli in clumps

Discussion

Hansen's disease is a chronic infectious disease with varied and atypical manifestations affecting the skin and peripheral nerves. A rare presentation of Hansen's disease is in the form of pure neuritic leprosy. It is characterized by sensory loss along the distribution of the nerve, with or without motor deficit. Neuropathy may be in the form of mononeuropathy, mononeuropathy multiplex, and/or polyneuropathy in the absence of cutaneous lesions [1, 2].

Three kinds of peripheral nerves are affected in leprosy:

- Superficially located dermal nerve twigs
- Superficially located cutaneous nerves
- Nerve trunks located deep to the deep fascia

Mycobacterium leprae enters the nerve in various ways. In the epidermis, lepra bacilli enter the naked nerve filaments and spread along the axons. Macrophages take up the lepra bacilli and aggregate around the nerve bundles. The bacilli are phagocytosed by the Schwann cells in the dermis. Trans-axonal spread of the bacilli occurs from the deep dermal and intradermal nerves to the unmyelinated nerves of the epidermis and deep dermis after which their axonal damage ensues [3]. Superficially placed nerves of cooler areas are easily traumatized.

Entrapment points in the fibro-osseous canals and the tight unyielding perineurium are also other sites of entry of the bacilli.

Neural involvement can manifest itself as enlargement of the superficial nerves such as great auricular, ulnar, median, radial cutaneous, superficial peroneal, sural, and posterior tibial which are clinically palpable against the corresponding bony prominences when thickened, associated with tenderness, in case of coexistent neuritis. Sensory impairment over the skin lesions is assessed by loss of sensation of temperature, touch, or pain. Nerve damage in leprosy may present itself as silent neuropathy without overt signs and symptoms or as a clinically manifest disease that may present as weakness, atrophy, or contracture. Glove and stocking pattern of sensory impairment results from damage to the type C fibers that carry heat and cold discrimination which is the earliest sensation lost during the disease. Touch sensation is lost subsequently followed by that of pain. Patients may complain of anhidrosis if there is associated sympathetic nerve involvement [4].

Indeterminate neuritis is the earliest manifestation of the disease where there is no functional and structural damage to the nerve. Nerve trunks are not involved. Clinically the patient complains of nagging pain enough to disturb the sleep [5].In tuberculoid neuritis usually, a single nerve is involved and may be characterized by nodular swelling and nerve abscess; caseous necrosis may occur [5, 6]. Axonal damage is the primary process in tuberculoid leprosy resulting as a bystander effect of destructive inflammatory process [7]. In lepromatous neuritis, since there are no immunity, bacilli slowly and steadily multiply with the gradual destruction of the nerve which is unnoticed till it is very late. As against the tubercular form, the lepromatous forms can show segmental myelin changes and relative preservation of axons in the initial stages irrespective of high bacillary load [7]. Numerous AFBs

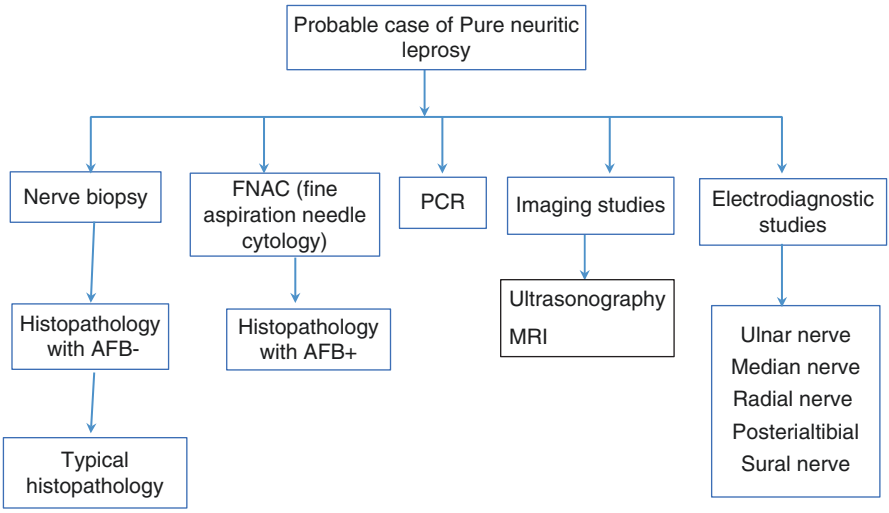

Fig. 18.2 Flowchart for investigation of pure neuritic leprosy

are seen in the Schwann cells, perineural cells, and macrophages. The infected nerve is seen surrounded by a macrophage granuloma. The nerve destruction is permanent and is replaced by fibrous tissue. In borderline neuritis, the extent of nerve paralysis is much more severe than all other forms and deformities are common.

The long incubation period of *Mycobacterium leprae*, the ability of leprosy to mimic other conditions, and low sensitivity of serological tests make clinical, histopathological, and nerve conduction studies and imaging studies necessary for the diagnosis of pure neuritic leprosy [1]. The algorithm for diagnosis of pure neuritic leprosy is depicted in Fig. 18.2 [5, 6].

In our case, we diagnosed the case as pure neuritic leprosy based upon clinical findings and cytology revealing AFB. The patient was treated with oral prednisolone 1 mg/kg body weight for 3 months following which there was a 70% improvement in weakness and foot drop. Subsequently slow tapering of prednisolone was done, and the patient was advised for foot care and physiotherapy. MDT MB (A) was prescribed for 12 months. In our case the symptoms started 1 year back which was misdiagnosed resulting in disability. We emphasize the role of detailed clinical examination, ultrasonography, and nerve conduction studies in early diagnosis and treatment of PNL to prevent progressive neural damage and complications.

References

1. Rao PN, Suneetha S. Pure neuritic leprosy: current status and relevance. Indian J Dermatol Venereol Leprol. 2016;82:252–61.
2. Payne R, Baccon J, Dossett J, et al. Pure neuritic leprosy presenting as ulnar nerve neuropathy: a case report of electrodiagnostic, radiographic, and histopathological findings. J Neurosurg. 2015;123:1238–43.

3. Hui M, Uppin MS, Challa S, et al. Resolving diagnostic issues in acid fast bacilli (AFB)-negative nerve biopsies: a single Centre experience from South India. Ann Indian Acad Neurol. 2015;18:292–7.
4. Kar S, Krishnan A, Singh N, et al. Nerve damage in leprosy: an electrophysiological evaluation of ulnar and median nerves in patients with clinical neural deficits: a pilot study. Indian Dermatol Online J. 2013;4(2):97–101.
5. Prasad PV, editor. All about leprosy. New Delhi: Jeypee Brothers Medical Publishers (P) Ltd.; 2005.
6. Einar WS. Diagnosis of pure neuritic leprosy. Neurol J Southeast Asia. 2002;7:61–3.
7. Ui M, Uppin MS, Challa S, et al. Pure neuritic leprosy: resolving diagnostic issues in acid fast bacilli (AFB)-negative nerve biopsies: a single Centre experience from South India. Ann Indian Acad Neurol. 2015;18:292–7.

Chapter 19
Asymptomatic Papules and Nodules Over the Body

Sunil Kumar Gupta

Abstract Histoid leprosy is a variant of lepromatous leprosy with a very bacillary load. This occurs due to dapsone monotherapy or de novo. Histoid leprosy clinically presents as firm, skin—coloured papules/nodules or plaques or sometimes with the myriad presentation. Very close observation is required to suspect histoid leprosy. Dermoscopy and characteristic histopathology confirm the diagnosis of histoid leprosy.

Keywords Histoid leprosy · Lepromatous leprosy · Histiocytes · Leproma · Fite—Faraco stain

Clinical Presentation

A 40–year-old male presented in the outpatient department with multiple papules all over the body for the last 1.5 years. He had consulted for this with different clinicians, but his problem was not resolved and his lesions were progressive. There was a history of numbness in his both hands and feet from the onset of the lesions. There was no history of fever, arthralgia, epistaxis or red eye. The bowel and bladder habit was normal.

On examination, there were multiple skin—coloured papules and nodules on the trunk and upper and lower limbs (Figs. 19.1, 19.2, and 19.3). The ears and face were also infiltrated with the same lesions (Figs. 19.4 and 19.5). All lesions were present on normal—looking skin. The lesions were firm and non—tender. There was no sensory loss in these lesions. Hypoesthesia was present on both hands and feet. None of the cutaneous nerve trunks was thickened or tender. The power of muscles of the eyes, hands and feet were within normal range. There was no visible deformity or ulcer.

S. K. Gupta (✉)
Department of Dermatology, AIIMS, Gorakhpur, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_19

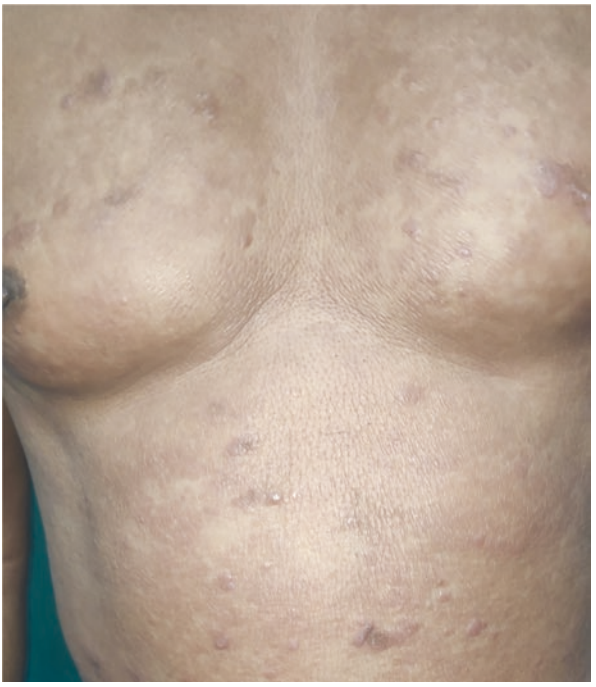

Fig. 19.1 Histoid leprosy—clinical: showing multiple firm skin-coloured papules on the chest and abdomen

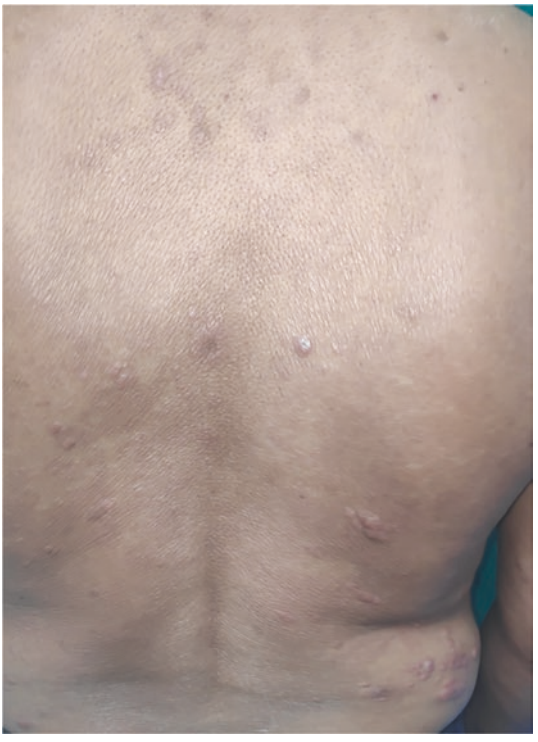

Fig. 19.2 Histoid leprosy—clinical: showing multiple firm skin-coloured papules on the back

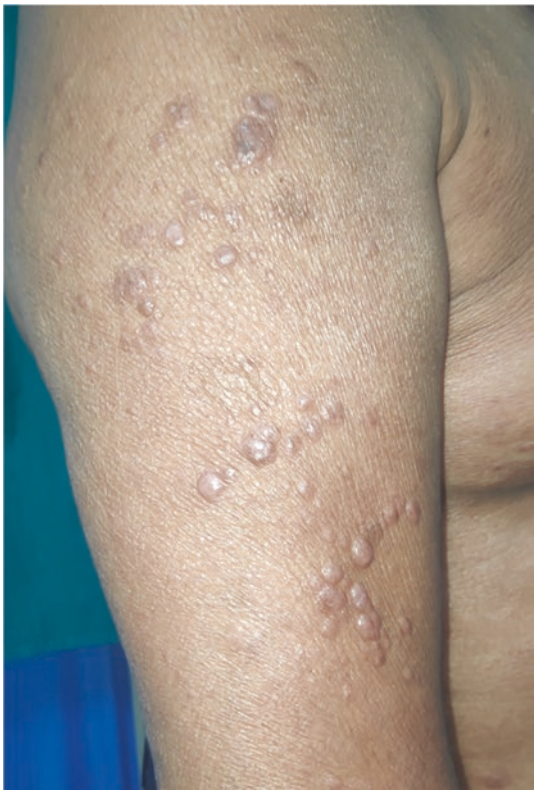

Fig. 19.3 Histoid leprosy—clinical: showing multiple firm skin-coloured papules on the arm

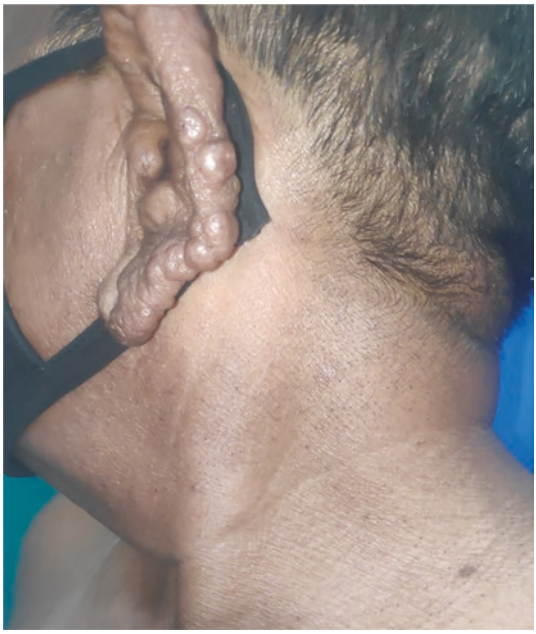

Fig. 19.4 Histoid leprosy—Clinical: showing multiple firm succulent papules infiltrating the ears

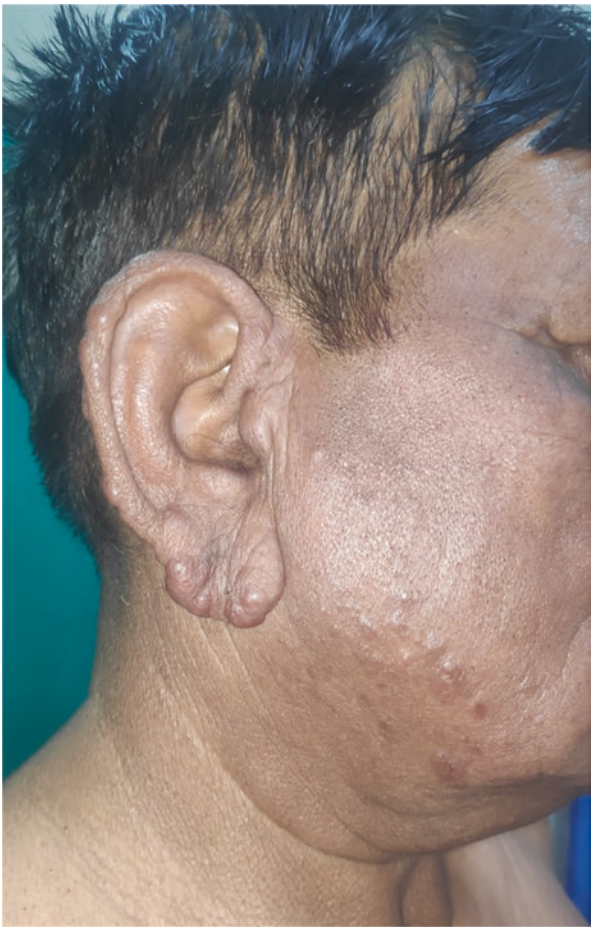

Fig. 19.5 Histoid leprosy—clinical: showing multiple skin-coloured papules on the face

What Is Your Diagnosis?

The following differentials were considered in the case:

1. Histoid leprosy.
2. Lepromatous leprosy.
3. Molluscum contagiosum.
4. Keloid.
5. Sarcoidosis.
6. Post—kala—azar dermal leishmaniasis.
7. Cutaneous T—cell lymphoma.

Investigations

Dermoscopy of the lesions revealed arborizing vessels on flesh—coloured, dome—shaped, shiny nodules over apparently normal skin with central umbilication (Fig. 19.6). Slit skin smear from the ear pinna showed globi. The complete blood count, liver function test and kidney function tests were within normal range. The VDRL test was non—reactive. The viral markers for HIV, hepatitis B and C and COVID-19 were also non—reactive. The rK39 test was also negative.

The histopathology of the lesion showed foamy histiocytes in the dermis (Fig. 19.7). Histoid leprosy was confirmed by the Fite—Faraco stain, which demonstrated the presence of AFB predominantly arranged in clumps within histiocytes (Fig. 19.8).

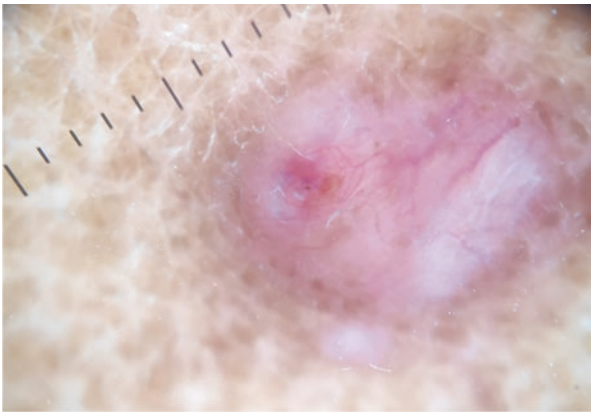

Fig. 19.6 Histoid leprosy—dermoscopy (DermLite 4™): showing arborizing vessels on flesh-coloured, dome-shaped, shiny nodules over apparently normal skin with central umbilication

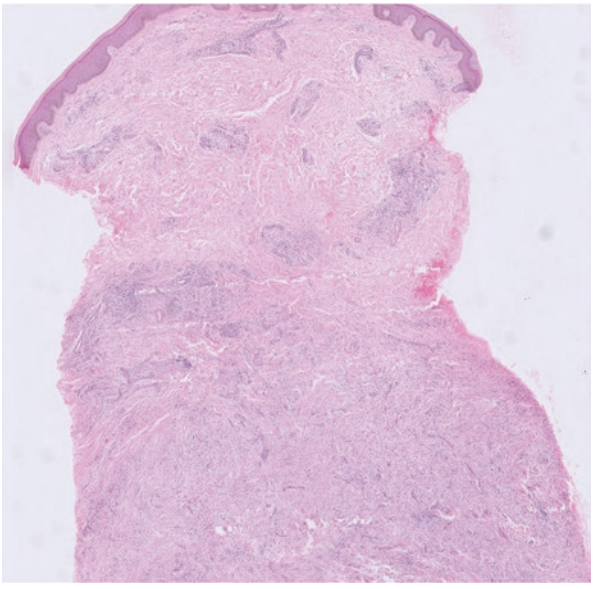

Fig. 19.7 Histoid leprosy—histopathology (H&E stain 10×): showing epidermal atrophy, green zone and foamy histiocytes in the dermis arranged in a whorled pattern

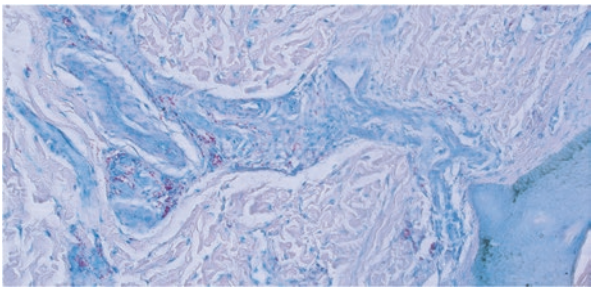

Fig. 19.8 Histoid leprosy—histopathology (Fite-Faraco stain 100×): showing presence of AFB predominantly arranged in clumps within histiocytes

Final Diagnosis

Histoid leprosy.

Discussion

A histoid leprosy is a form of lepromatous leprosy that may develop at any stage of disease course or de novo [1]. It is highly bacillated which requires early diagnosis and management. It was first described by Dr. Herbert Windsor Wade in the 1960s [2]. The data regarding global prevalence of histoid leprosy is still lacking. The incidence in India has been reported to vary from 2.79 to 3.60% among total leprosy patients [3]. There is male preponderance, and the average age at diagnosis is between 21 and 40 years [2]. A review article reported that the incidence of histoid leprosy was 8.7% among lepromatous leprosy [4].

Histoid leprosy can occur during dapsone monotherapy or even when there is no history of inadequate or irregular treatment. The etiopathogenesis is not well established. There is a hyperactive immune response in multibacillary leprosy to localize the lesions that result in the development of histoid leprosy. This response includes an increased cluster of differentiation 36 (CD36) expression by keratinocytes, CD4 T lymphocytes, B lymphocytes and immunoglobulin levels. However, macrophages seem to lack the functionality to kill *M. leprae* bacteria present in high numbers in the histoid lesions [5]. The humoral immunity was found to be enhanced as evidenced by the increased absolute count of B lymphocytes and raised levels of immunoglobulins IgG, IgM and IgA [6].

Histoid leprosy is clinically characterized by painless, firm, cutaneous and/or subcutaneous papules, nodules or plaques with well—defined edges and a smooth bright surface [2]. Papules and nodules were the most common skin lesions. The lesions are usually located on the posterior and lateral aspects of the arms, dorsum of the hands, back, buttocks, thighs, legs and over bony prominences such as the elbows and knees, with a localized asymmetric pattern and arising from apparently normal—looking skin [4]. In contrast, classical LL presents with generalized symmetric lesions that arise from infiltrated skin [7]. Atypical skin lesions, such as

tumour—like masses, molluscum contagiosum—like lesions, xanthoma—like, prurigo nodularis—like mucosal and genital lesions, have been reported and may mislead the diagnosis of histoid leprosy [4, 8]. Nerve affectation, leading to anaesthetic lesions or sensory impairment to temperature, touch or pain, may be mild or absent. Sometimes, the lesions of sarcoidosis, post—kala—azar dermal leishmaniasis, keloid, dermatofibroma, neurofibroma, molluscs contagiosum, deep mycosis and mycosis fungoides mimic like histoid. An eagle eye is required to rule out these dermatological conditions.

The diagnosis of histoid leprosy is suspected clinically, supported by dermoscopy and confirmed by a typical histopathological picture with the demonstration of AFB in Fite—Faraco stain.

Dermoscopy may help in the diagnosis of histoid leprosy. The characteristic finding is linear branching vessels and shiny white structures or multiple, flesh—coloured, dome—shaped, shiny, nodules over apparently normal skin with central umbilication, transepidermal elimination and signs of pseudo—koebnerization in a few lesions [9, 10].

Typical histopathological findings include epidermal atrophy with a sub—epidermal acellular band, known as the grenz zone. The leproma is contained within the dermis and is a well—circumscribed area consisting of spindle—shaped histiocytes arranged in an intertwining, whorled or storiform pattern and surrounded by a pseudocapsule. An abundance of characteristic lepra bacilli, within histiocytes, arranged singly, in clumps, or rarely as globi under the Fite—Faraco stain helps to confirm the diagnosis [2, 4].

The standard treatment of histoid leprosy is MB—MDT. As with other leprosy cases, early detection and appropriate treatment are encouraged to prevent future disabilities and stop disease transmission. We started MB—MDT for our patient.

We should keep in mind that the histoid form could serve as a reservoir of leprosy and as a source of new cases. This could pose a serious threat to our elimination program [11].

References

1. Sehgal VN, Srivastava G. Histoid leprosy a review. Int J Dermatol. 1985;24:286–92.
2. Wade HW. The histoid variety of lepromatous leprosy. Int J Lepr. 1963;31:129–42.
3. Annigeri SR, Metgud SC, Patil JR. Lepromatous leprosy of histoid type. Indian J Med Microbiol. 2007;25:70–1.
4. Gupta SK. Histoid leprosy: review of the literature. Int J Dermatol. 2015;54(11):1283–8.
5. Kaur I, Dogra S, De D, Saikia UN. Histoid leprosy: a retrospective study of 40 cases from India. Br J Dermatol. 2009;160(2):305–10.
6. Rao AG. Borderline tuberculoid leprosy associated with histoid leprosy. Indian J Dermatol. 2016;61(5):580. https://doi.org/10.4103/0019-5154.190130.
7. Piedrahíta-Rojas LM, Díaz CJ, Escandón-Vargas K. De novo histoid leprosy in a Colombian patient with multiple skin nodules on the ears and extremities. Rev Soc Bras Med Trop. 2019;52:e20160502. https://doi.org/10.1590/0037-8682-0502-2016.

8. Nawalerspanya S, Sangmala S, Aiempanakit K. A case report of Prurigo Nodularis-like lesions in a patient with lepromatous leprosy. Case Rep Dermatol. 2020;12(3):236–40.
9. Acharya P, Mathur MC. Clinicodermoscopic study of histoid leprosy: a case series. Int J Dermatol. 2020;59(3):365–8. https://doi.org/10.1111/ijd.14731.
10. Mohta A, Jain SK, Agrawal A, Kushwaha RK, Sharma P, Sethia K, Jain M. Dermoscopy in leprosy: a clinical and histopathological correlation study. Dermatol Pract Concept. 2021;11(2):e2021032. https://doi.org/10.5826/dpc.1102a32.
11. Palit A, Inamadar AC. Histoid leprosy as reservoir of the disease; a challenge to leprosy elimination. Lepr Rev. 2007;78:47–9.

Chapter 20
An Asymptomatic Swelling on the Right Arm

Nibedita Patro and Biswanath Behera

Abstract An adult male presented with a solitary asymptomatic nodule on the arm demonstrating hypoaesthesia along the nerve distribution on clinical examination. After routine necessary investigations, it was diagnosed as a case of pure neuritic leprosy in the multibacillary spectrum involving a single nerve trunk and was treated with multibacillary multidrug therapy. Histopathological examination of the peripheral nerve is the gold standard for diagnosis. In resource poor settings apart from following the current NLEP guidelines for therapeutic purpose, a multibacillary approach is recommended in doubtful cases regarding the number of nerves involved. An early diagnosis and overtreatment are quite justifiable while dealing with pure neuritic leprosy so as to prevent the morbid deformities.

Keywords Pure neuritic leprosy · Multibacillary leprosy · Asymptomatic swelling · Hypoaesthesia

Clinical Presentation

A 24–year-old male presented with an asymptomatic swelling on the right arm for 4 months. He denied any history of prior trauma at the site of the swelling. There was no personal or family history of leprosy. On clinical examination (Fig. 20.1), a solitary 1×2 cm^2 size skin—coloured, subcutaneous, firm, non—tender nodule was noted. It was attached to a thickened cord—like structure when palpated peripherally along the radial nerve direction. The nodule was mobile and could be rolled along with the cord. Hypoaesthesia could be elicited over the nodule extending

N. Patro (✉)
Department of Dermatology, Venereology and Leprology, Hi-Tech Medical College and Hospital, Bhubaneswar, India

B. Behera
Department of Dermatology, Venereology and Leprology, AIIMS, Bhubaneswar, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_20

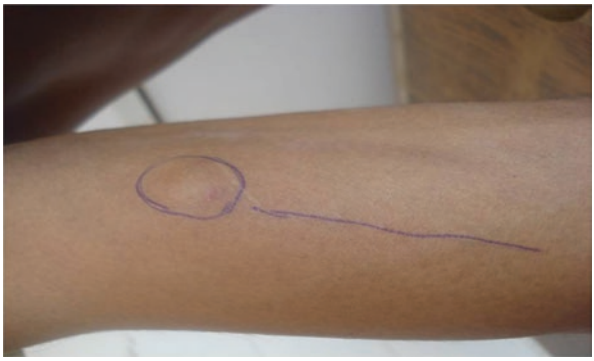

Fig. 20.1 Single subcutaneous firm nodule attached to a cord-like structure on the right arm near the elbow

along the radial nerve distribution in the right forearm and hand. The right radial cutaneous nerve (RCN) near the wrist was enlarged compared to the left side. There was no associated nerve tenderness, any other peripheral nerve enlargement, or hypopigmented skin lesion. Other mucocutaneous, general and systemic examinations were within normal limits.

What Is Your Diagnosis?

(a) Neurofibroma.
(b) Pure neuritic leprosy.
(c) Lipoma.
(d) Calcinosis cutis.

Investigations

All routine blood parameters including complete blood count, liver function and renal function tests were within normal range. A slit skin smear for acid—fast bacilli (AFB) from both ear lobes and the skin over the nodule was negative. The nerve conduction study (NCS) (Fig. 20.2) elicited a decreased sensory conduction velocity in the right radial nerve. A fine needle aspiration cytology (FNAC) smear (Fig. 20.3) from the nodule showed predominantly epithelioid cells. The histopathological study of nerve biopsy specimen (Fig. 20.4) from the right RCN demonstrated marked epineurial and perineurial thickening, dense endoneurial inflammation with loss of myelination and infiltration of histiocytes including the foamy ones. Fite—Faraco stain was positive for AFB (Fig. 20.5).

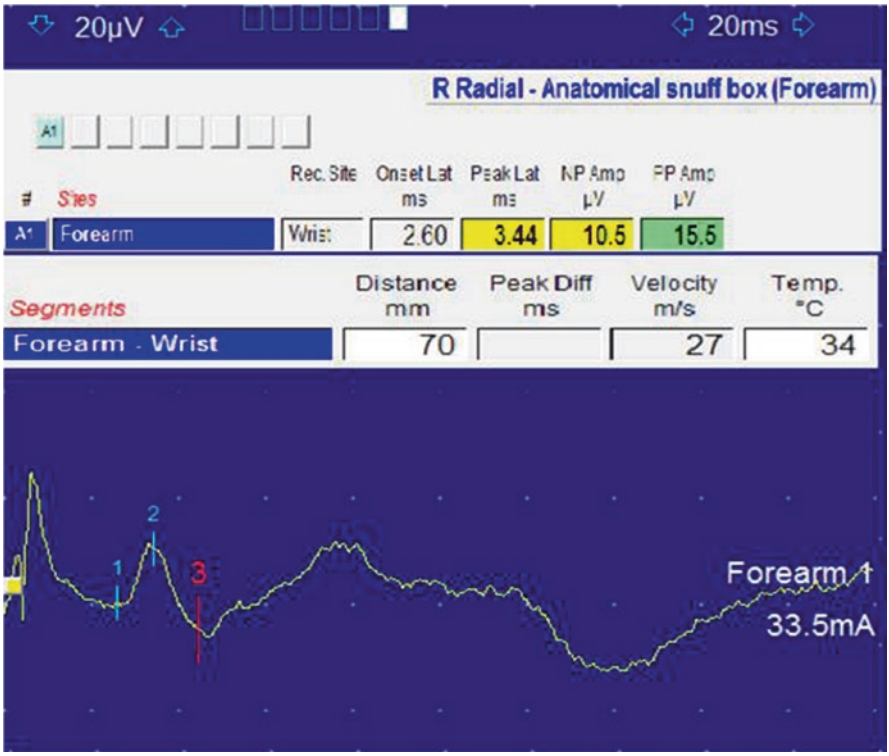

Fig. 20.2 Nerve conduction study of the right radial nerve showing slowing of sensory conduction velocity in the forearm

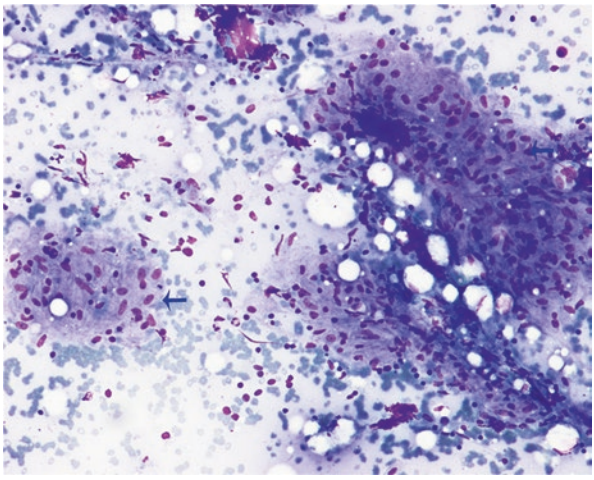

Fig. 20.3 Cellular smear shows multiple well-formed epithelioid granulomas admixed with few reactive lymphocytes (MGG stain, ×400)

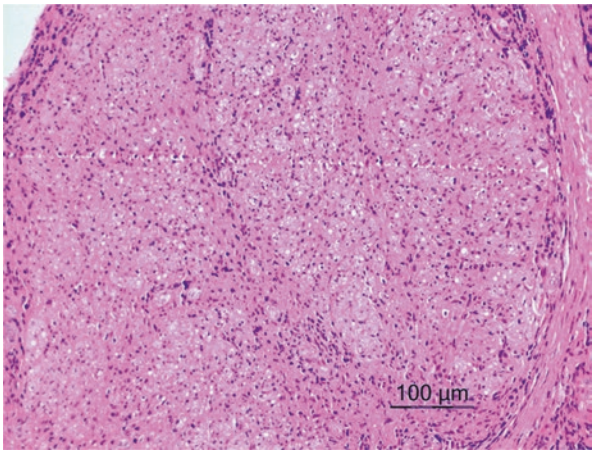

Fig. 20.4 Dense endoneurial inflammation with loss of myelination and infiltration of histiocytes (Hematoxylin & Eosin, ×200), asterix – epineural thickening, arrows – foamy histiocytes

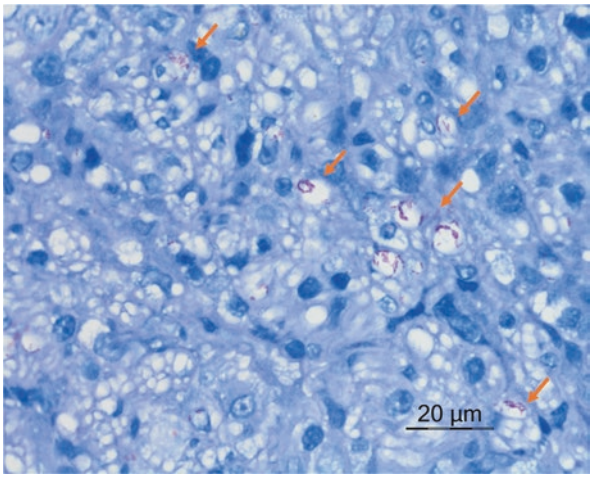

Fig. 20.5 Fite-Faraco stain showing solid AFB

Final Diagnosis

The final diagnosis of pure neuritic leprosy in the multibacillary spectrum was made.

Discussion

The first mention of the neural form of leprosy called “lepra nervorum” was made by Albert Neisser in 1930 [1]. It was later on included as a subtype called “neuritic leprosy” among the different types of leprosy at the International Leprosy Congress, Madrid, in 1953. The Indian Association of Leprologists (IAL) recognized this distinct entity officially as “polyneuritic leprosy” in 1955, which was later on renamed

as “pure neuritic leprosy” in 1982. Pure neuritic leprosy (PNL) can be defined as leprosy affecting single or multiple nerves, without skin lesions. The former can present as thickening of large nerve trunks or their branches, with sensory loss along the distribution of the affected nerve and negative skin smears for AFB [2].

PNL accounts for 5.5–18% of total cases of leprosy in India [3–5]. It is more commonly seen in men [6] and has been found to affect people from 15 to 60 years age group [6, 7]. Mononeuritis predominantly involving the upper limb nerves is the commonest presentation [8]. Ulnar nerve in the upper limb and lateral popliteal nerve in the lower limb are the common nerves affected, followed by posterior tibial and sural nerves. Symmetric polyneuritis is uncommon in PNL and should be carefully evaluated for lepromatous leprosy [8]. The sudden appearance of numbness with or without ulcers, deformity, or muscle weakness in a limb is the most common presentation. Nerve pain (neuropathic pain) has also been reported [9, 10]. Clinically, the nerve is significantly thickened and can be nodular or beaded, and rarely abscess (cold abscess) formation is observed. The skin changes like hypo/anhidrosis, xerosis, fissuring and ulceration may be seen depending on the severity of sensory and autonomic dysfunction. Patients may also present with neuritis at the time of presentation or develop during multidrug therapy [3]. In some cases, “silent neuritis” or “quiet nerve paralysis” leading to various deformities (claw hand, foot drop, trophic ulcer) can be the initial presentation [6].

The histopathological study of the nerve is considered the gold standard for confirmation of PNL. The presence of AFB in either Schwann cells or macrophages is an unequivocal finding in PNL. In cases with negative AFB, epithelioid granulomas in the endoneurial compartment suggest a high probability of leprosy. The presence of epineurial infiltrate, endoneurial infiltrate, endoneurial fibrosis and decreased number of myelinated nerve fibres can differentiate PNL from other non—leprous neuropathies [11, 12]. A study from South India [13] demonstrated a spectrum of pathological features in nerve biopsies, ranging from lepromatous to tuberculoid leprosy, and a significant number of these patients (46%) demonstrated features of multibacillary leprosy. Histopathological examination of skin biopsies from the normal—looking skin along the distribution of the nerve can demonstrate features of leprosy, including epithelioid and macrophage granuloma, in around one—third cases [14]. Similarly, nasal mucosa biopsy can demonstrate features of leprosy, even before other manifestations. A study showed specific features of leprosy like nerve inflammation, epithelioid and macrophage granuloma including AFB, in around 50% cases [15].

FNAC, a safe, rapid and less invasive procedure have demonstrated the following features in the nerve fibres:AFB, epithelioid granulomas, Langhans giant cells and chronic inflammatory cells [16–18]. However a negative aspirate does not rule out leprosy. Polymerase chain reaction (PCR) assays targeting different *Mycobacterium leprae* genes like sodA, 16S ribosomal RNA, RLEP and Ag 85B have been tried on nerve aspirates with 100% specificity. However, the sensitivity is 50% and 100% in paucibacillary and multibacillary cases, respectively [19, 20].

Slowing of sensory conduction velocity and changes in latency are observed in nerve conduction studies of leprosy patients. Compared to magnetic resonance

imaging (MRI), high—resolution ultrasonography has been more efficient, economical and user—friendly and detects nerve enlargement even in subclinical cases. The findings of nerve thickening, enlarged fascicles, epineural thickening and increased endo—and epineural blood flow in HRUS suggest leprous neuropathy [21, 22].

Our patient was started on multibacillary multidrug therapy (MB MDT) based on the investigational findings. The treatment guidelines for PNL as a distinct type of leprosy are yet to be defined. Currently the National Leprosy Eradication Programme (NLEP) guidelines are being followed for therapeutic purposes. Studies have suggested considering cutaneous nerve twigs involvement and anatomical location of nerve involvement while choosing the appropriate multidrug therapy [23], and in doubtful cases regarding the number of nerves involved, multibacillary approach is advisable [8]. Others suggest that the therapeutic decisions in PNL cases should be guided by histologic findings rather than the number of nerve involvement [24], as different studies have found lepromatous histology in mononeuropathic presentations and vice versa [24, 25]. The episodes of acute neuritis as well as silent neuropathy need early identification and management to prevent deformities. Tricyclic antidepressants and anticonvulsants help in managing neuropathic pain [26, 27]. Finally, teaching self—care of the anaesthetic limbs and early physiotherapy and corrective procedures for the deformities are of utmost importance.

Acknowledgement We are sincerely thankful to Dr. Suvendu Purkait, Associate Professor, Department of Pathology, AIIMS Bhubaneswar, for the histopathology image, and Dr. Subhransu Sekhar Jena, Assistant Professor, Department of Neurology, Hi—Tech Medical College, Bhubaneswar, for the NCS image.

References

1. Prasad PV, editor. All about leprosy. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2005.
2. Cinical histopathological and immunological features of the five type classification approved by the Indian association of leprologists. Lepr India. 1982;54:22–5.
3. Kumar B, Kaur I, Dogra S, Kumaran MS. Pure neuritic leprosy in India:rAn appraisal. Int J Lepr Other Mycobact Dis. 2004;72:284–90.
4. Narang T, Vinay K, Kumar S, Dogra S. A critical appraisal on pure neuritic leprosy from India after achieving WHO global target of leprosy elimination. Lepr Rev. 2016;87:456–63.
5. Sasidharanpillai S, Reena Mariyath OK, Riyaz N, Binitha MP, George B, Janardhanan AK, et al. Changing trends in leprosy among patients attending a tertiary care institution. Indian J Dermatol Venereol Leprol. 2014;80:338–40.
6. Mendiratta V, Khan A, Jain A. Primary neuritic leprosy: a reappraisal at a tertiary care hospital. Indian J Lepr. 2006;78:261–7.
7. Kolleri JJ, Sasidharanpillai S, Vadakkayil B, Chathoth AT. A 10-year retrospective descriptive study on pure neuritic leprosy from a tertiary referral Centre. Indian Dermatol Online J. 2019;10:13–8.
8. Rao PN, Suneetha S. Pure neuritic leprosy: current status and relevance. Indian J Dermatol Venereol Leprol. 2016;82:252–61.

9. Al Suwaid AR, Venkatram MN, Banodkar DD. Study of pure neuritic leprosy in Oman. Gulf J Dermatol. 1994;1:25–7.
10. Jardim MR, Antunes SL, Santos AR, Nascimento OJ, Nery JA, Sales AM, et al. Criteria for diagnosis of pure neural leprosy. J Neurol. 2003;250:806–9.
11. Antunes SL, Chimelli L, Jardim MR, Vital RT, Nery JA, Corte-Real S, et al. Histopathological examination of nerve samples from pure neural leprosy patients: obtaining maximum information to improve diagnostic efficiency. Mem Inst Oswaldo Cruz. 2012;107:246–53.
12. Hui M, Uppin MS, Challa S, Meena AK, Kaul S. Pure neuritic leprosy: resolving diagnostic issues in acid fast bacilli (AFB)-negative nerve biopsies: a single Centre experience from South India. Ann Indian Acad Neurol. 2015;18:292–7.
13. Suneetha S, Arunthathi S, Kurian N, Chacko CJ. Histological changes in the nerve, skin and nasal mucosa of patients with primary neuritic leprosy. Acta Leprol. 2000–2001; 12. 11–18.
14. Kumar B, Kaur I, Dogra S, Kumaran MS. Pure neuritic leprosy in India: an appraisal. Int J Lepr Other Mycobact Dis. 2004;72:284–90.
15. Suneetha S, Arunthathi S, Job A, Date A, Kurian N, Chacko CJ. Histological studies in primary neuritic leprosy: changes in the nasal mucosa. Lepr Rev. 1998;69:358–66.
16. Jayaseelan E, Shariff S, Rout P. Cytodiagnosis of primary neuritic leprosy. Int J Lepr Other Mycobact Dis. 1999;67:429–34.
17. Kumar B, Pradhan A. Fine needle aspiration cytology in diagnosis of pure neuritic leprosy. Pathol Res Int. 2011;2011:158712.
18. Vijaikumar M, D'Souza M, Kumar S, Badhe B. Fine needle aspiration cytology (FNAC) of nerves in leprosy. Lepr Rev. 2001;72:171–8.
19. Martinez AN, Ribeiro-Alves M, Sarno EN, Moraes MO. Evaluation of qPCR-based assays for leprosy diagnosis directly in clinical specimens. PLoS Negl Trop Dis. 2011;5:e1354.
20. Bang PD, Suzuki K, Phuong le T, Chu TM, Ishii N, Khang TH. Evaluation of polymerase chain reaction-based detection of mycobacterium leprae for the diagnosis of leprosy. J Dermatol. 2009;36:269–76.
21. Jain S, Visser LH, Praveen TL, Rao PN, Surekha T, Ellanti R, et al. High-resolution sonography: a new technique to detect nerve damage in leprosy. PLoS Negl Trop Dis. 2009;3:e498.
22. Jain S, Visser LH, Yerasu MR, Raju R, Meena AK, Lokesh B, et al. Use of high resolution ultrasonography as an additional tool in the diagnosis of primary neuritic leprosy: a case report. Lepr Rev. 2013;84:161–5.
23. Handa S, Dogra S. Hot topics in leprosy. Lepr Rev. 2003;74:87–8.
24. Shukla B, Verma R, Kumar V, Kumar M, Malhotra KP, Garg RK, Malhotra HS, Sharma PK, Kumar N, Uniyal R, Pandey S, Rizvi I. Pathological, ultrasonographic, and electrophysiological characterization of clinically diagnosed cases of pure neuritic leprosy. J Peripher Nerv Syst. 2020;25:191–203.
25. Kulshreshtha D, Malhotra KP, Malhotra HS, et al. Mandating nerve biopsy: a step towards personalizing therapy in pure neuritic leprosy. J Peripher Nerv Syst. 2018;23:190–6.
26. Rao PN, Suneetha S. Neuritis-definition, clinico-pathological manifestations and proforma to record nerve impairment in leprosy. In: Kar HK, Kumar B, editors. IAL textbook of leprosy. 1st ed. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2010. p. 253–68.
27. Haanpää M, Lockwood DN, Hietaharju A. Neuropathic pain in leprosy. Lepr Rev. 2004;75:7–18.

Chapter 21
A Female with Erythematous Plaques Over the Face and Trunk

Dependra Kumar Timshina

Abstract Recognition of type 1 reaction in leprosy is paramount for the early detection, prevention, limitation, and management of disabilities. These reactions are expressed as inflammatory skin lesions and nerve damage resulting in sensory and motor deficits. We are describing a 42-year-old female who presented with sudden onset of erythematous plaques over the face and trunk along with acral edema. She was diagnosed as a case of borderline tuberculoid leprosy with type 1 reaction by clinical and histopathological correlation.

Keywords Type 1 reaction · Reversal reaction · Borderline tuberculoid · Borderline lepromatous · Immunity

Clinical Presentation

A 42-year-old female, shopkeeper by occupation, presented with complaints of multiple red raised lesions over the face and trunk for 3 months, with pain over a few lesions. The patient had noted swelling of the feet for around 1 month. There was a history of pain over the elbow predominantly over the right side for 2 weeks. She also had a few hypopigmented areas over the face and trunk for around 6 months. The patient was on MBMDT (multibacillary multidrug therapy) for the last 5 months from a primary health center. She was also on oral contraceptives irregularly. On clinical examination, there were multiple, erythematous, edematous, and swollen plaques with well—defined borders over the chin, malar area, forehead, and trunk (Fig. 21.1). The plaques were red, prominent, swollen, and smooth looking and had sharp margins. Similar plaques were also noted over the trunk. Few lesions were tender on tapping. Surface temperature appeared to be raised over a few plaques. Decreased sensation to touch and the pain was seen in the extremities and over a few

D. K. Timshina (✉)
Remedy Clinics, Siliguri, West Bengal, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_21

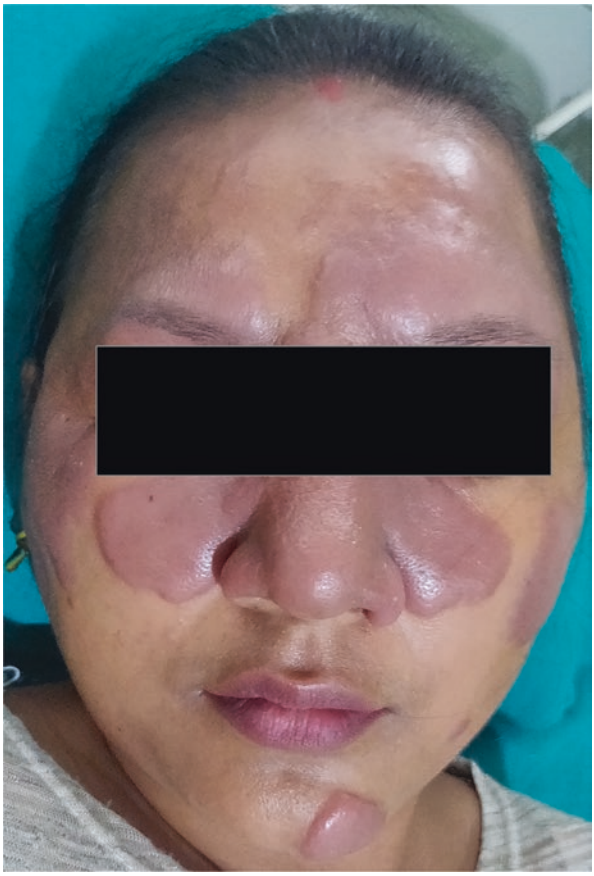

Fig. 21.1 Reversal reaction showing erythematous, edematous well-defined plaques over the chin, malar area, and forehead

lesions. There was edema in both legs. The right ulnar nerve was thickened, palpable with mild tenderness.

What Is Your Diagnosis?

- Hansen's disease with type 1 reaction (reversal reaction).
- Mycosis fungoides.
- Sarcoidosis.
- Lupus erythematosus (subacute).

Investigations

- Serology for HIV and hepatitis B and hepatitis C was non—reactive.
- Total leukocyte count was raised.
- ANA screening was negative.
- Slit skin smear from the eyebrows, earlobes, dorsum of the hand, and the lesional areas did not show any acid—fast bacilli.
- Skin biopsy from the red raised plaque over the face showed epidermis atrophy with upper dermis edema with moderate to dense infiltrate of lymphocytes, histiocytes, epithelioid cells, few foreign body giant cells with occasionally neutrophil around perivascular, periappendageal, and perineural with interstitial spill. There was no Pautrier's microabscess, mucin, and basement membrane thickening (Fig. 21.2).

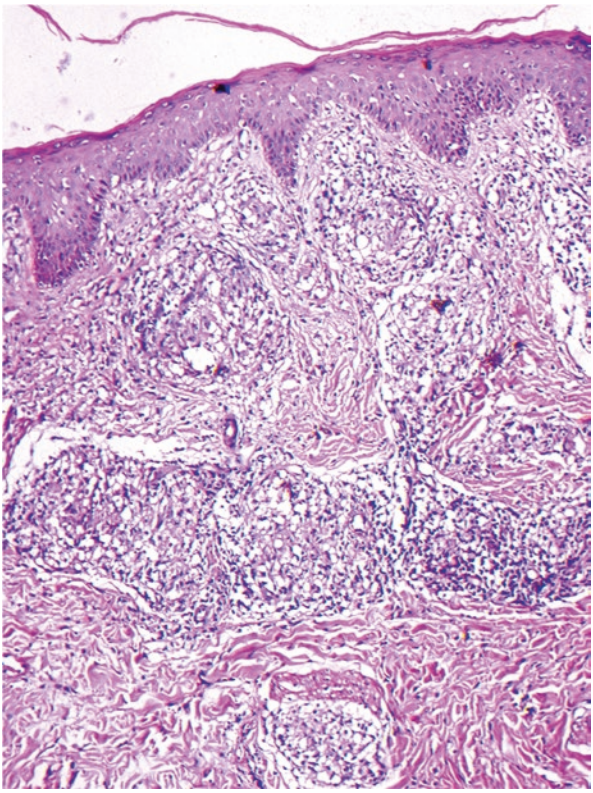

Fig. 21.2 Skin biopsy from the facial plaque shows multiple variably sized well-defined epithelioid cell granulomas in the superficial and mid-dermis. The granulomas are reaching up to the papillary dermis. Edema is evident within the granulomatous foci. Langhans giant cell is seen in the mid-dermal granulomatous foci (H&E × 100)

Final Diagnosis

Borderline tuberculoid leprosy with type 1 lepra reaction.

Discussion

Reactions in leprosy are acute inflammatory episodes superimposed on the relatively uneventful course of leprosy [1]. They occur following treatment or spontaneously and may be seen in up to 50% of leprosy patients. Lepra reactions assume importance because of their ability to damage the nerve trunks leading to disability, deformities, and morbidities [2]. Lepra reactions are mainly divided into type 1 reaction (reversal reaction, RR) and type 2 reaction (erythema nodosum leprosum, ENL). WHO classification (Ridley and Jopling 1996), showing the main type of reactional episode arising in each clinical form, is depicted in Table 21.1 [2].

Predisposing factors for the increased risk are summarized in Box 21.1 [3–5].

Box 21.1
- Initiation of therapy.
- Borderline leprosy.
- Immunization.
- HAART in HIV patients.
- Female gender, oral contraceptives, postpartum state.
- Neuritis past or present.
- Hepatitis B and C infections.
- Anti—PGL-1 (anti—Phenolic glycolipid-1) antibodies.
- Lepromin positivity.

Reversal reactions or type 1 reactions occur commonly in patients with borderline leprosy who are immunologically unstable. Rarely do patients with lepromatous leprosy also develop reversal reactions. These reactional episodes are associated with increased Th1 cellular immune response with movement towards the tuberculoid pole of disease, hence the name. Consequently, there is a vigorous host response against *M. leprae* in the skin and nerves, with local production of interferon-γ and tumor necrosis factor combined with the effects of cytolytic CD4+ T cells.

Clinical features include erythema, edema over preexisting skin lesions, and appearance of new skin lesions. Severe cases may show surface scaling or ulceration. There may be acral edema and dactylitis. Most cases have associated neuritis which is the leading cause of motor deformities and disability in the affected. There is often a diagnostic dilemma to differentiate true relapse from a late reversal reaction [3]. The differentiating features of both conditions have been described in Table 21.2.

Table 21.1 Clinical forms of leprosy and the reactional episodes arising in each clinical form

Leprosy type	TT	BT	BB	BL	LL
Reactional episode		RR	RR	RR	
				ENL	ENL

Table 21.2 Reversal reaction vs relapse

Conditions	Reversal reactions	Relapse
Type of leprosy	Seen in BT, BB, BL, LL subpolar	All types of leprosy
Time	Sudden onset and anytime during treatment, usually within 6 months	Slow onset, usually after 6 months to 3 years after completion of treatment
Skin	Erythema, edema, pain, scaling, rarely new lesions	New lesions present
Nerves	Pain, tenderness, inflammation may be present	Not involved
Steroids	Response is good	Steroids therapy not very effective

Our patient was already diagnosed as a case of borderline tuberculoid leprosy and was on MB MDT for 5 months, and she was also on OCPs irregularly. She developed type 1 reaction on preexisting skin lesions along with right ulnar neuritis. She was diagnosed as BT leprosy with type 1 lepra reaction basing upon clinical and histopathological findings. She was treated with 40 mg prednisolone for 2 weeks and tapered subsequently over 3 months. The erythema, edema, and neuritis improved completely. Early diagnosis of type 1 lepra reaction is of paramount importance to prevent progressive nerve damage and thereby deformities. All the patients should be counseled regarding the features of lepra reaction at the time of diagnosis so that they can present early to the physician for the prompt treatment.

References

1. Prasad PV, editor. All about leprosy. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2005.
2. Nery JA, BernardesFilho F, Quintanilha J, Machado AM, Oliveira Sde S, Sales AM. Understanding the type 1 reactional state for early diagnosis and treatment: a way to avoid disability in leprosy. An Bras Dermatol. 2013;88(5):787–92.
3. Kar HK, Sharma P. IAL textbook of leprosy. 1st ed. New Delhi: Jaypee brothers medical publishers(P) Ltd.; 2010. p. 289.
4. PathaniaV SD, Shankar P, Matharu YS, Baveja V. Two atypical presentations of lepra reactions. Int J Mycobacteriol. 2018;7(4):390–3.
5. Roche PW, Theuvenet WJ, Britton WJ. Risk factors for type-1 reactions in borderline leprosy patients. Lancet. 1991;338(8768):654–7.

Chapter 22
Erythematous Plaques over Photo Exposed Areas

Swetalina Pradhan and Ratnakar Shukla

Abstract Patients with leprosy and lepra reaction can have varied presentation; type 1 reaction is an acute event clinically characterised by exacerbation of skin lesion, inflammation of nerves, or both; if undetected, these acute episodes can lead to serious disabilities, deformities and morbidity; therefore, prompt recognition of reaction episodes in Hansen's disease is very essential for efficient management; herein, we present a case of a 45-year-old lady who presented with reddish lesions distributed predominantly in photo—exposed areas for which leprosy in type 1 reaction, sweet syndrome, SCLE, and EM were kept as differentials. However, histopathology confirmed a diagnosis of Hansen's disease with type 1 reaction. The lesions were strikingly limited over sun—exposed areas. This case represents a rare instance of photo—distributed borderline tuberculoid Hansen's with type 1 reaction.

Keywords Leprosy · Lepra reaction · Sweet syndrome · Subcutaneous lupus erythematosus · Erythema multiforme

Clinical Presentation

A 45-year-old married Hindu female residing and hailing from Patna, Bihar, presented with chief complaints of reddish—coloured skin lesions associated with burning pain predominantly distributed over photo—exposed areas since the last 15 days. The lesions started suddenly over the face and subsequently involved bilateral arms, right shoulder, 'V' area of the neck, and upper back within a span of 15 days. There were no associated systemic symptoms. The patient denied a history of any drug intake prior to the onset of skin lesions. There was no significant personal and family history as well. Cutaneous examination revealed erythematous to hyperpigmented and oedematous plaques varying in size from 1 × 1 cm to 10 × 8 cm on photo—exposed areas (Fig. 22.1a–d). Majority of the lesions were of round to

S. Pradhan (✉) · R. Shukla
Department of Dermatology, All India Institute of Medical Sciences, Patna, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_22

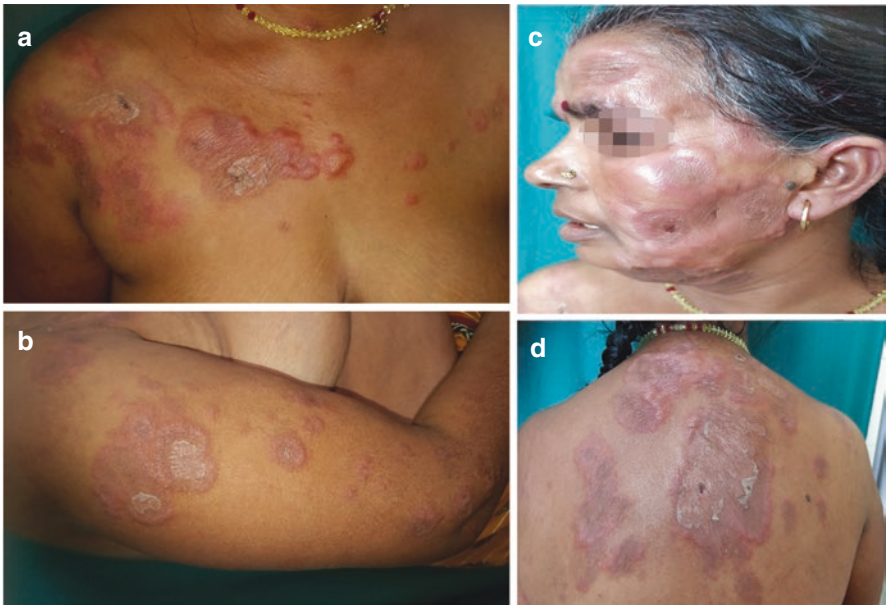

Fig. 22.1 (**a**) Multiple erythematous and oedematous plaques in photo—exposed areas at initial presentation. (**b**) Erythematous and edematous plaque with scaling on surface over right arm. (**c**) Targetoid appearance over the face. (**d**) Polycyclic appearance over the back

oval with few giving targetoid (Fig. 22.1c) and polycyclic appearance (Fig. 22.1d) over the face and upper back, respectively. Majority of the plaques had scaling on the surface with pigmentary changes. The lesions were tender on palpation. Apart from the above skin lesions, a single hypopigmented, ichthyotic, hypoesthetic patch of size 2 × 2 cm was noted on the left forearm which was present for 1 year as told by the patient, and for the same, she took paucibacillary (PB) multidrug therapy (MDT) irregularly for 7 months. The left ulnar nerve was thickened (grade 1) and tender (grade 1). The rest of the peripheral nerves were within normal limits; no motor deficits were found on examination. The palms, soles, and mucosa were apparently normal. Patient's general and systemic examination was found to be normal.

What Is Your Diagnosis?

a. Erythema multiforme with borderline tuberculoid leprosy.
b. Subacute cutaneous lupus erythematosus with borderline tuberculoid leprosy.
c. Sweet syndrome with borderline tuberculoid leprosy.
d. Borderline tuberculoid leprosy with type 1 lepra reaction.

Investigations

All routine haematological and urinary investigations were within normal range. The patient's autoimmune profile was negative. Slit skin smears (from ear lobe and a plaque on arm) showed 2+ bacilli index. Histopathological study from the plaque over the right cheek and upper back showed granuloma consisted of foamy macrophages and lymphocytes, multifocal granulomatous infiltrate in superficial and deep dermis and composed of Langhans giant cells, epitheloid cells and cuffed by lymphocytes. The dermo—epidermal junction was spared by the granulomatous infiltrate (Fig. 22.2). These findings were consistent with the diagnosis of borderline tuberculoid Hansen's disease with type 1 reaction (T1R).

Final Diagnosis

Borderline tuberculoid leprosy with type 1 lepra reaction.

Discussion

Lepra reactions are immunological phenomena and major cause of morbidity in leprosy [1]. Type 1 lepra reactions can be either upgrading or downgrading. Upgrading reactions are also called as reversal or false exacerbation reaction, mostly seen within 6 months of starting therapy, whereas downgrading reaction is associated with disease worsening. Type 1 lepra reactions can occur in the skin, nerves, or

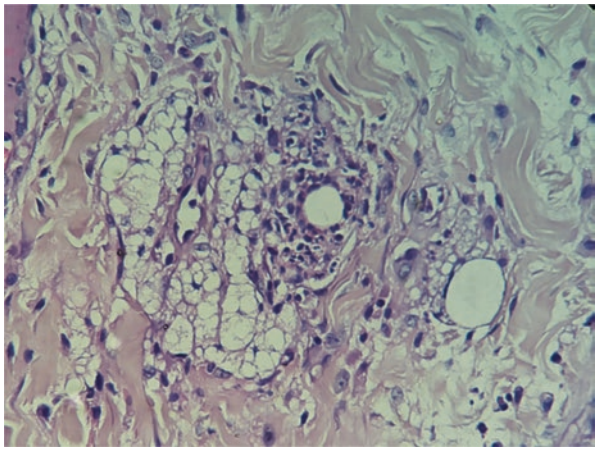

Fig. 22.2 Perivascular lymphocytic infiltrate and foamy macrophages (H&E × 400)

both and are often associated with neuritis. If left untreated, neuritis in type 1 reactions can lead to permanent loss of nerve function and deformity [2]. Risk factors which can trigger type 1 lepra reaction include initiation of therapy, pregnancy, parturition, puberty, intercurrent infections, stress, trauma, use of oral contraceptives, increasing age, and extensive disease although they also occur without any clear inciting event [3, 4]. Early administration of corticosteroids is essential to preserve nerve function in type 1 reactions and prevent limb deformity and disability [3]. Typically, type 1 reactions present as sudden onset of erythema and oedema over pre—existing skin lesions along with appearance of new skin lesions with or without neuritis [5]. However, sometimes T1LR may present in an atypical manner as in our case. Herein, the patient was presented with sudden onset of painful tender erythematous, oedematous, round, oval, targetoid, polycyclic plaques predominately over photo—exposed areas along with associated scaling and pigmentary changes in the majority of the lesions for which sweet syndrome, SCLE, and EM were kept as differentials. However, histopathology from the erythematous plaques over the face and upper back was contributory to BT Hansen's disease with T1R. After confirmation of diagnosis, the patient was started on 1 mg/kg of oral prednisone for the treatment of her type 1 reaction along with calcium, vitamin D, and a proton pump inhibitor. MDT adult pack MB regiment for 12 months duration was included in her therapy. After 15 days of treatment with prednisolone, all the erythematous plaques resolved (Fig. 22.3a–d).

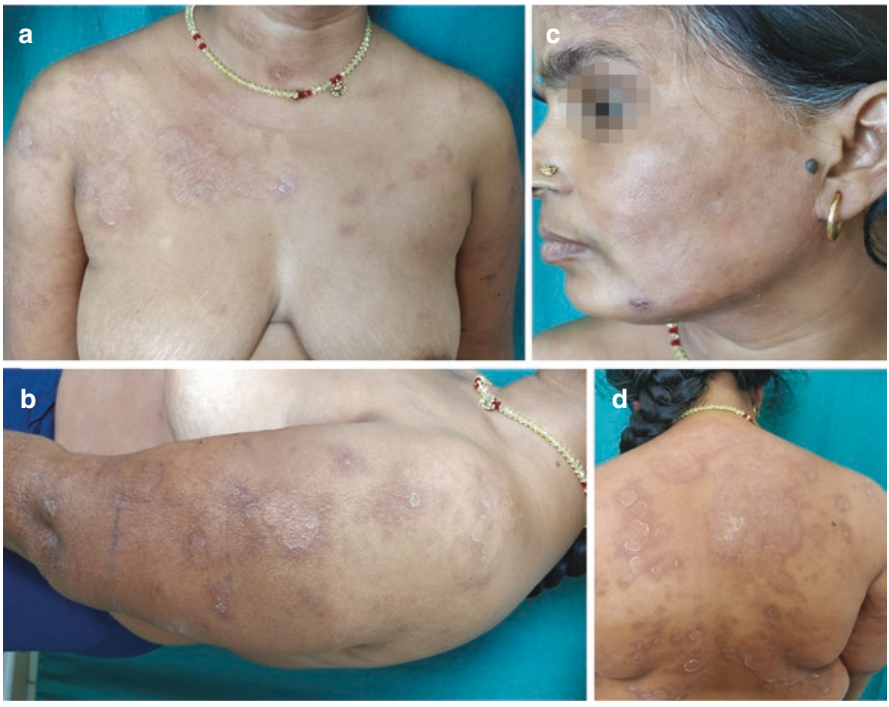

Fig. 22.3 (**a–d**) Multiple plaques in healing phase after treatment

T1R with varied morphology of skin lesions presenting over photo—exposed areas has been rarely reported in the literature. Hence, in an endemic area of leprosy, a high index of suspicion for Hansen's disease is warranted for such atypical presentation to avoid delay in diagnosis and treatment.

References

1. Pandhi D, Chhabra N. New insights in the pathogenesis of type 1 and type 2 lepra reaction. Indian J Dermatol Venereol Leprol. 2013;79(6):739–49.
2. Van Brakel WH, Khawas IB, Lucas SB. Reactions in leprosy: an epidemiological study of 386 patients in West Nepal. Lepr Rev. 1994;65(3):190–203.
3. Nery JA, Bernardes Filho F, Quintanilha J, Machado AM, Oliveira Sde S, Sales AM. Understanding the type 1 reactional state for early diagnosis and treatment: a way to avoid disability in leprosy. An Bras Dermatol. 2013;88(5):787–92.
4. Kumar B, Dogra S, Kaur I. Epidemiological characteristics of leprosy reactions: 15 years' experience from North India. Int J Lepr Mycobact Dis Off Organ Int Lepr Assoc. 2004;72(2):125–33.
5. Scollard DM, Adams LB, Gillis TP, Krahenbuhl JL, Truman RW, Williams DL. The continuing challenges of leprosy. Clin Microbiol Rev. 2006;19(2):338–81.

Chapter 23
Painful Nodules and Cribriform Scars on the Body

Chandra Sekhar Sirka and Kananbala Sahu

Abstract Erythema nodosum leprosum (ENL) lesions may be confused with a wide range of dermatosis. Specially, failure to diagnose lepromatous leprosy because of its poor visibility on clinical examination may pause a diagnostic challenge for ENL. We are discussing a case of ENL which was misdiagnosed as cutaneous small vessel vasculitis for its morphological similarity. However, hypoesthesia at lesional site, glove and stocking anaesthesia, sagging earlobes with infiltration, and gynaecomastia lead to clinical suspicion of lepromatous leprosy and type 2 lepra reaction (ENL), which was later confirmed by slit skin smear examination and histopathology.

Keywords Erythema nodosum leprosum · ENL · Type 2 reaction · Cutaneous vasculitis · Cribriform scar

Clinical Presentation

A 56-year-old male presented to dermatology OPD with episodes of painful reddish nodules and scars of varying stages over limbs for 5 months (Fig. 23.1). The episode of nodular eruption was associated with fever and joint pain. Biopsy from lesion was suggestive of IgA vasculitis from outside, and the patient was treated with systemic prednisolone at varying doses. However, each time the effort to taper prednisolone below 30 mg resulted in recurrence. Prolonged prednisolone use had caused Cushingoid appearance, striae, and cataract in the patient.

General examination revealed mild pallor and bilateral pitting oedema of the hands and feet. Dermatological examination revealed multiple erythematous to

C. S. Sirka (✉)
Department of Dermatology, All India Institute of Medical Sciences, Bhubaneswar, India

K. Sahu
Department of Dermatology, Sri Jagannath Medical College and Hospital, Puri, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_23

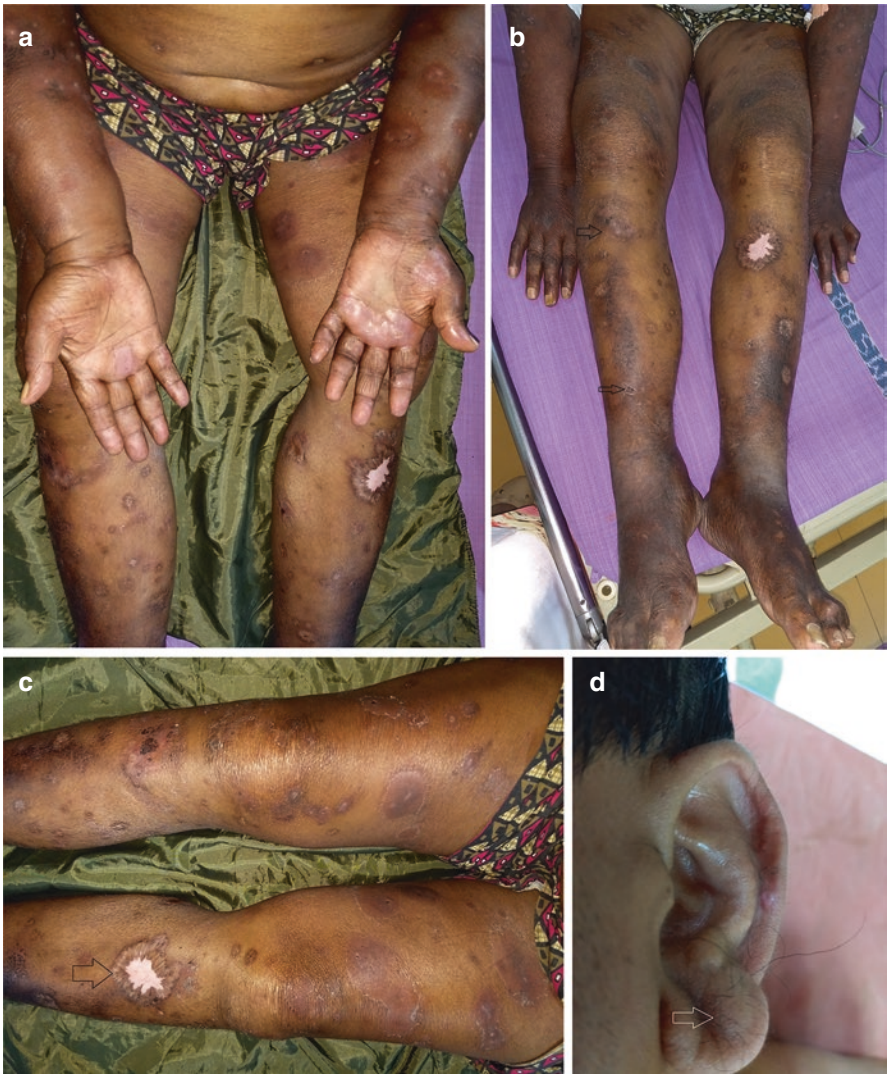

Fig. 23.1 (**a**) Erythematous nodules and plaques over the limbs with massive oedema. (**b**) Nodules and plaques with central ulceration. (**c**) Healed lesions showing cribriform scars over the limbs. (**d**) Sagging of earlobes with infiltration

skin—coloured plaques and nodules of size ranging from 1 × 2 to 3 × 4 cm^2 over the limbs and few lesions over the trunks. Some lesions had ulcerated at the centre (Fig. 23.1b). The healed scars were circular and had cribriform wrinkled pigmented skin over it (Fig. 23.1c). He also had sagging earlobes with infiltration (Fig. 23.1d) and gynaecomastia. Further cutaneous examination revealed 5–10% loss of sensation on the nodules, healed scars, and glove and stocking anaesthesia on extremities. Bilateral ulnar and common peroneal nerves were thickened.

What Is Your Diagnosis?

- Cutaneous small vessel vasculitis.
- Urticarial vasculitis.
- Sweet syndrome.
- Necrotic erythema nodosum leprosum.

Investigations

Baseline investigations were within normal limits. Slit skin smear was positive with bacterial index (5+). Histopathology showed a grenz zone along with plenty of foamy macrophages in dermis (Fig. 23.2a–c). The special staining for AFB was positive (Fig. 23.2d). Dermis showed perivascular infiltration and endothelial swelling.

Final Diagnosis

Lepromatous leprosy with necrotic erythema nodosum leprosum (erythema necroticans).

Discussion

Erythema nodosum leprosum (ENL) or type 2 reaction is an immune complex—mediated hypersensitivity reaction. It occurs mainly in lepromatous or borderline lepromatous leprosy [1]. Skin lesions of ENL typically present with superficial or deep, erythematous, tender papules or nodules. They heal within 7–10 days with post—inflammatory hyperpigmentation. Besides the typical lesion, ENL may present with pustular, bullous [2], ulcerated [3], and erythema multiforme—like lesions [4, 5]. Rarely, sweet syndrome—like [6–10], vasculitis—like [11], and PLEVA—like [12] morphology of ENL has been reported in the literature.

Suspicion or diagnosis of leprosy is from the cardinal sign. The cardinal sign includes hypopigmented, hypoaesthetic patch, thick and/or tender nerve, and positive acid—fast bacilli in slit skin smear. In the absence typical features diagnosis may be confirmed by clinic—histopathological correlation. In the above elaborated case, the initial histological finding confused the physician for IgA vasculitis and misled the management. Near similar, misdiagnosis of ENL for vasculitis was reported by Bhattacharjee et al. [11] In the present case though ENL was confused for vasculitis and sweet syndrome. Cutaneous examination revealed sagging

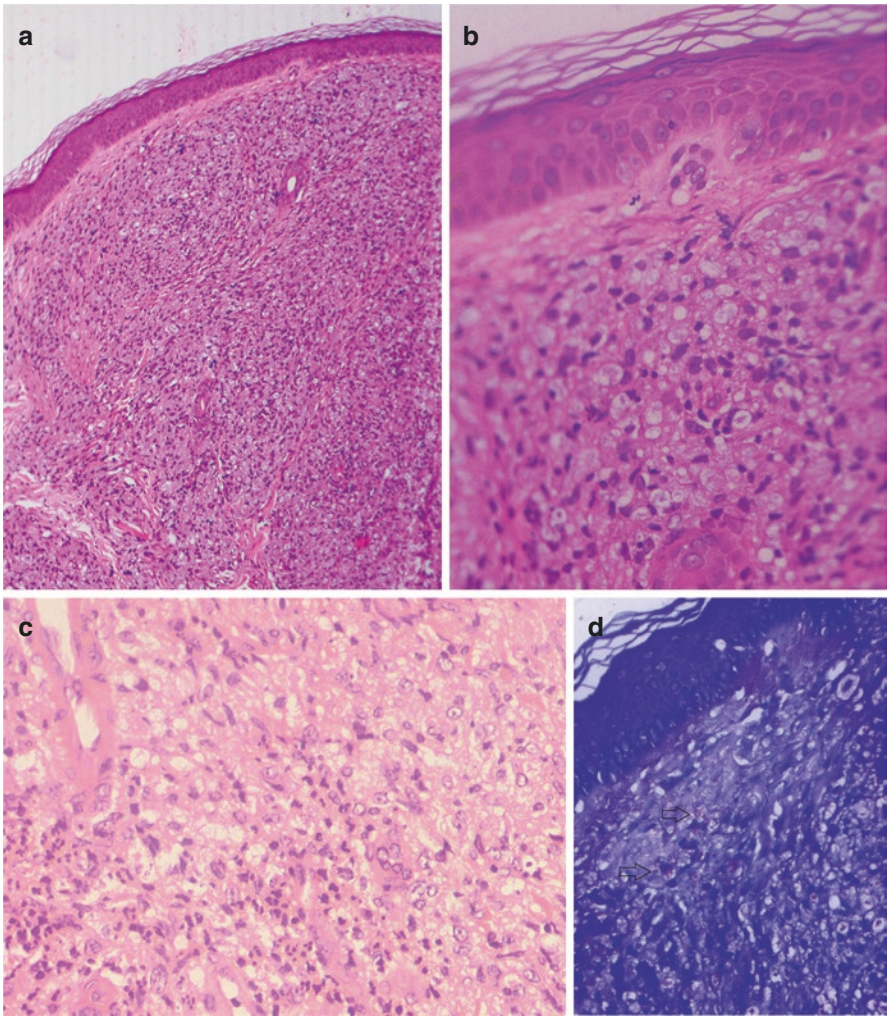

Fig. 23.2 (**a**) Low-power view showing grenz zone and lymphohistiocytic infiltration of the dermis (40 × H&E). (**b** and **c**) High-power view showing foamy histiocytes infiltration of the dermis and endothelial swelling (400 × H&E). (**d**) Acid-fast staining showing clumps of bacilli

earlobes, hypoesthesia on ENL lesions, glove and stocking anaesthesia, and gynaecomastia which was in favour of lepromatous leprosy in our case and was later on supported by investigations. Hence author argue, that clinico-histopathological correlation may be ideal to reach at a diagnosis in doubtful and poorly responding patients.

Treatment of ENL includes treatment of leprosy with WHO MDT multibacillary adult's regimen and control of reaction with corticosteroid, thalidomide, and clofazimine.

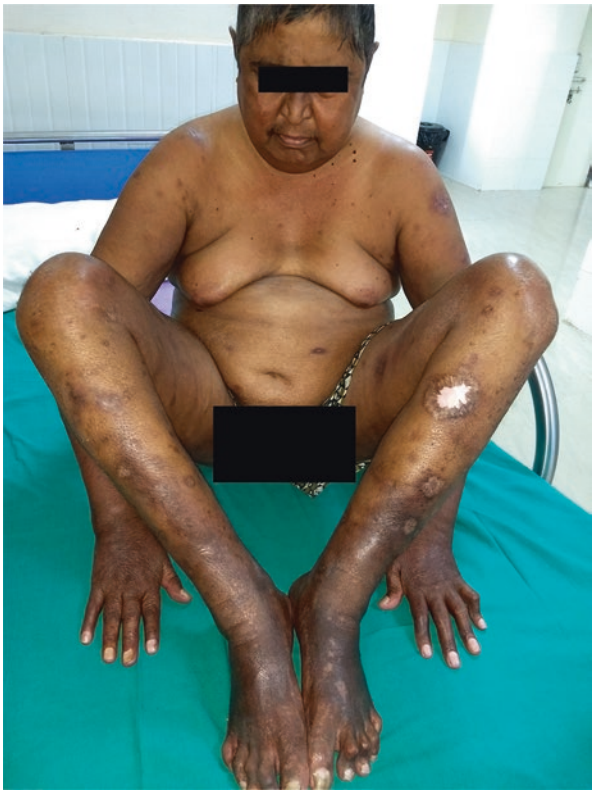

Fig. 23.3 Improvement of lesions,2 weeks after oral steroid and thalidomide

Our patient was started with WHO MDT—MB(A) along with systemic oral prednisolone 1 mg/kg body weight and thalidomide 400 mg daily for control of reaction (Fig. 23.3). The prednisolone was tapered 5 mg every 2 weeks while he was on thalidomide. Now the patient is on follow—up for more than 6 months without any recurrence.

The case is being discussed to highlight the varied presentation of erythema nodosum leprosum and importance clinic-histopathological correlation.

References

1. Walker SL, Balagon M, Darlong J, et al. An international multi-centre cross-sectional study of the clinical features of erythema nodosum leprosum. PLoS Negl Trop Dis. 2015;9:(e0004065).
2. Pradhan S, Rout AN, Sirka CS, Sahu K, Dash G. Bullous erythema nodosum leprosum: a rare case series. Lepr Rev. 2019;90:469–75.
3. Sirka CS, Panda M, Pradhan S, Baisakh MR. Necrotic erythema nodosum leprosum healing with extensive scars. Indian. Dermatol Online J. 2017;8:509–11.
4. Miranda AM, Antunes SL, Nery JA, et al. Erythema multiforme in leprosy. Mem Inst Oswaldo Cruz. 2012;107:34–42.
5. Sabrina S, Andrade João G, Maroclo SAL, et al. An unusual presentation of leprosy at diagnosis: erythema multiforme-like type 2 reaction. Revista de Patologia Tropical. 2010;39:221–7.
6. Heng Y-K, Chiam Y-TL, Giam Y-C, Chong W-S. lepromatous leprosy in erythema nodosum leprosum reaction mimicking Sweet's syndrome. Int J Dermatol. 2011;50:1124–5.
7. Kuo TT, Chan HL. Severe reactional state in lepromatous leprosy simulating Sweet's syndrome. Int J Dermatol. 1987;26:518–20.
8. Aires NB, Reflkalefsky LW, Villela MA, et al. Sweet's syndrome type leprosy reaction. J Eur Acad Dermatol Venereol. 2009;23:467–9.
9. Das T, Ghosh S, Kundu AK, Maity A. Reactional state in lepromatous leprosy simulating Sweet's syndrome. J Assoc Physicians India. 2013;61:856–8.
10. Chiaratti FC, Daxbacher EL, Neumann AB, Jeunon T. Type 2 leprosy reaction with sweet's syndrome-like presentation. An Bras Dermatol. 2016;91:345–9.
11. Bhattacharjee R, Chatterjee D, Narang T, Dogra S. Necrotic erythema nodosum leprosum masquerading as cutaneous vasculitis. Rheumatology. 2019;1(58):85.
12. Sirka CS, Sahu K, Pradhan S, Naik S, Rout AN, Dash G. Erythema nodosum leprosum (ENL) mimicking Pityriasis lichenoides et varioliformis acuta (PLEVA): an atypical presentation. Lepr Rev. 2018;2018(89):310–5.

Chapter 24
Generalized Painful Erythematous Nodules

Tanmay Padhi and Paraini Marandi

Abstract A 34-year-old male presented with painful red swellings of 1 week duration. He was also having fever and joint pain. The eruptions were episodic in nature. On examination, he had painful erythematous nodules all over the body with pus formation and ulceration over many of them. His ear lobules and face had non-tender infiltrated nodules. Right ulnar and common peroneal nerves were enlarged and tender. Slit skin smear examination and histopathology confirmed the diagnosis of necrotic erythema nodosum leprosum.

Keywords Necrotic erythema nodosum leprosum · Infiltrated nodule · Slit skin smear

Clinical Presentation

A 34-year-old male, agricultural worker by profession, presented to the outpatient department with fever, joint pain, and painful red swellings all over the body of 7 days duration. The patient gave a history of similar eruptions twice before the present attack. He had sought treatment with the local hospital in his village where he was treated with different oral and injectable antibiotics and analgesics. The first two episodes were much milder and had subsided within a week of starting treatment. The present attack was much more severe with high-grade fever and chills and severe joint pain over his elbows, knees, ankles, and small joints of his hands which did not respond to the treatment offered at his native place. Moreover, most of the swellings had become pus filled. There was no history of long-term fever, cough, weight loss, or joint pain. He never had any skin eruptions following

T. Padhi (✉) · P. Marandi
Department of Dermatology, VSS Institute of Medical Sciences and Research, Sambalpur, Odisha, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_24

exposure to sunlight. He was also not intolerant to any medications. However, he did have stuffiness of the nose with occasional bleeding and some abnormal sensations over his hands and feet.

The patient was hospitalized, and a thorough general and dermatological examination was conducted. He had fever, mild pallor, and pedal edema. The rest of the systemic examinations did not reveal any abnormalities.

The cutaneous findings were very prominent. He had numerous nodules all over his face, trunk, and extremities. Ear lobules looked infiltrated. While lesions over the face were less inflamed evidenced by lack of pain, tenderness, and surrounding erythema (Fig. 24.1a, b), those on the trunk and extremities were painful and tender. Most of the nodules over the trunk had a pustule at their tops though some had ulcerated and crusted at the time of presentation suggesting different stages of evolution (Figs. 24.2a, b and 24.3). Almost all of them had intense erythema surrounding them (Fig. 24.4). In between the painful nodules, there were some plaques and nodules which were neither painful nor tender. The patient described them to be present long before the appearance of the painful eruptions.

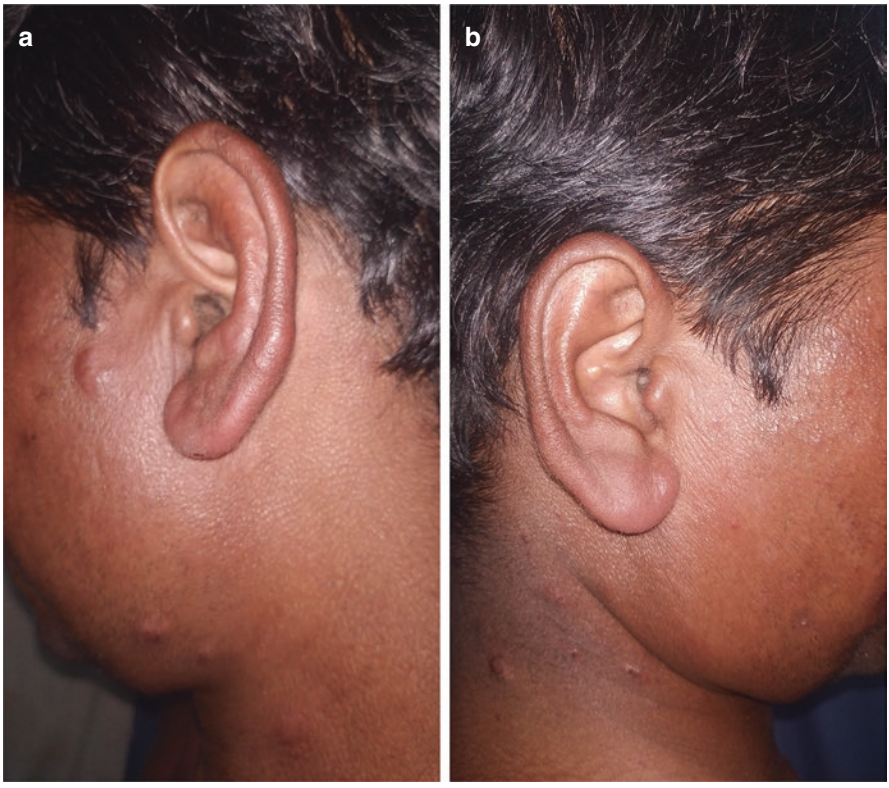

Fig. 24.1 (**a**, **b**) Non-inflammatory nodules over the face and ear lobules

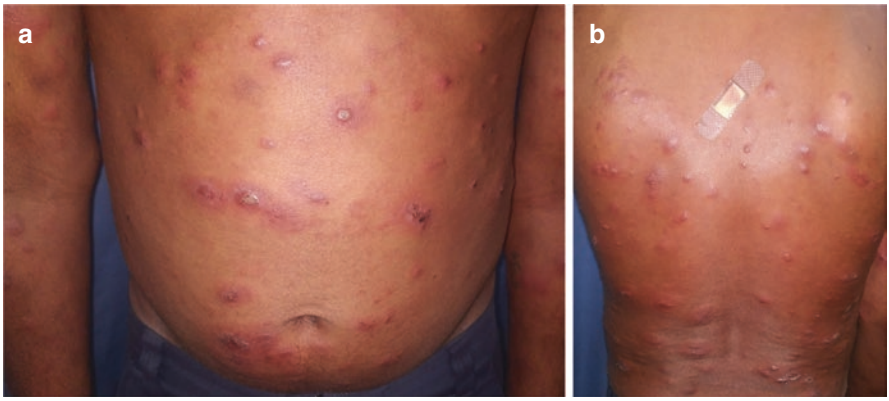

Fig. 24.2 (**a**, **b**) Pustular, ulcerated, and crusted nodules over the trunk with few non-inflammatory lesions

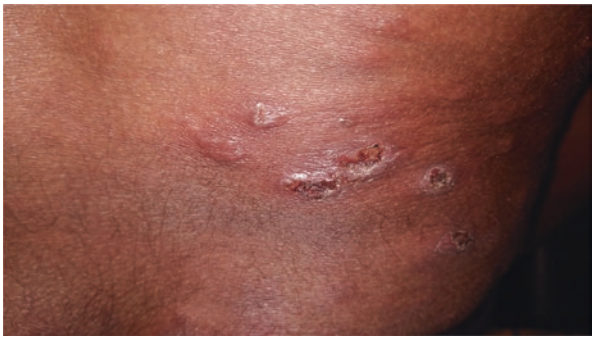

Fig. 24.3 Pustular, ulcerated, and crusted nodules over the upper arm with perilesional erythema

Right ulnar and right common peroneal nerves were enlarged and tender. Sensory loss to fine touch was present over the dorsum of the hands and feet. There was no evidence of any deformities or non-healing ulcer.

What Is Your Diagnosis?

1. Polyarteritis nodosa (cutaneous vasculitis).
2. Lupus panniculitis.
3. Erythema nodosum leprosum.
4. Papulonecrotic tuberculid.

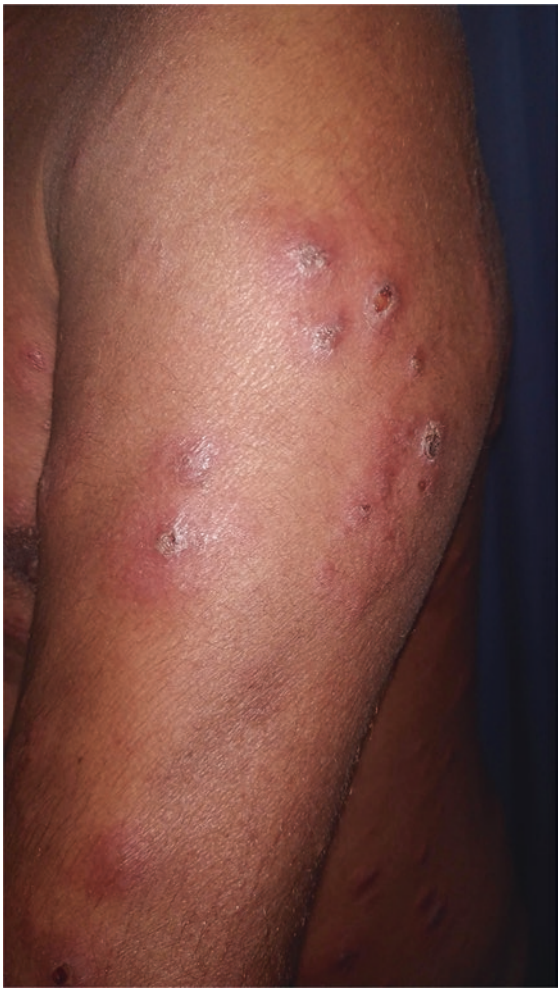

Fig. 24.4 Close-up view of an ulcerated nodule on the back

Investigations

The patient was subjected to routine hematological investigations. The significant positive findings were leukocytosis (12,400/mm^3), neutrophilia (82%), raised absolute neutrophil count (8800/mm^3), and raised ESR (37 mm/first hr). Antinuclear antibody was negative. Results for C-ANCA and P-ANCA were negative. Test for antinuclear antibody (ANA) was also negative.

Slit skin smear for AFB from ear lobules showed plenty of *Mycobacterium leprae*. Many of the bacilli were arranged in groups (Fig. 24.5).

Biopsy from a nodule on the back showed foamy macrophages, epithelioid cells, and giant cells (Fig. 24.6a, b). There was dense neutrophilic aggregation in the dermis, more prominent towards the deeper layer (Fig. 24.7).

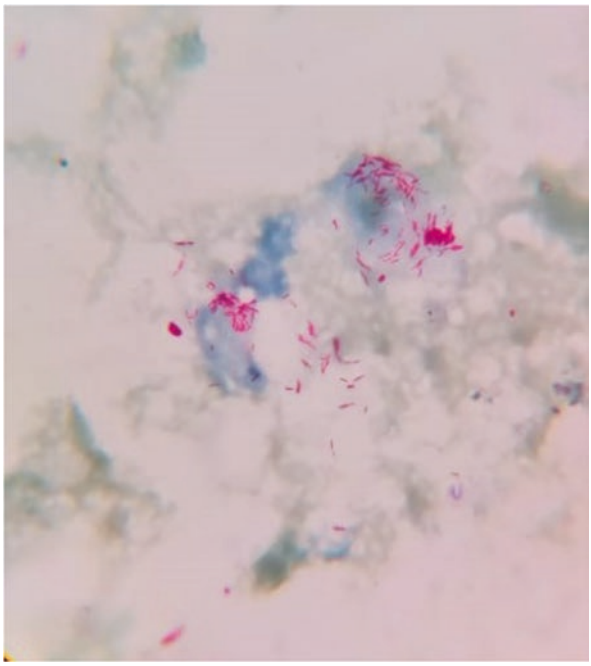

Fig. 24.5 *Mycobacterium leprae* arranged in groups (slit skin smear) (oil immersion ×1000)

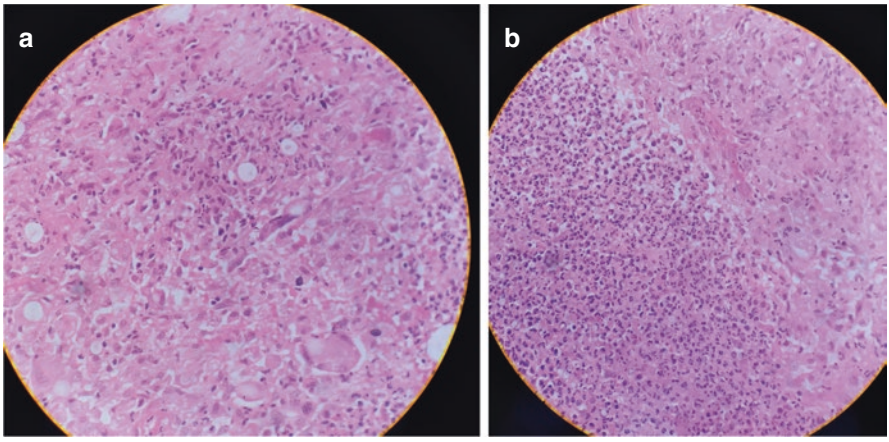

Fig. 24.6 (**a, b**) Foamy macrophages, giant cells, and epithelioid cells (H&E × 400)

Final Diagnosis

Lepromatous leprosy with necrotic erythema nodosum leprosum (ENL).

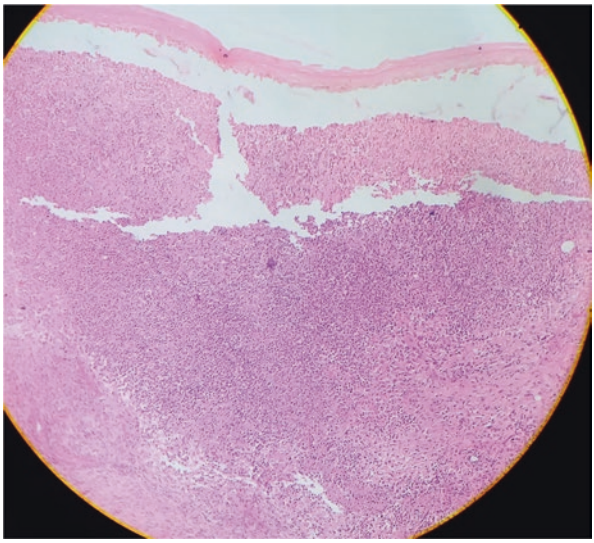

Fig. 24.7 Dense neutrophilic infiltration in deeper dermis (H&E × 100)

Discussion

Even after India had declared leprosy to be eliminated officially, it is a fairly common disease in some of the endemic pockets of the country [1]. The western part of Odisha is one such area. In the post-elimination era, the number of multibacillary cases, particularly the highly bacilliated variants, is being reported in significant numbers.

Erythema nodosum leprosum, also known as type 2 lepra reaction, is commonly seen towards the lepromatous pole. Immune complex deposition, cell-mediated immunity, and T-cell-mediated inflammation have been thought to be the pathogenetic mechanisms behind this condition [2]. The disease is a great mimicker with many clinical features shared with conditions like lupus panniculitis, polyarteritis nodosa, and papulonecrotic tuberculid. It is a multisystem disease affecting the bones and joints, eyes, lymph nodes, kidneys, testes, etc. Necrotic ENL, a variant of ENL, where the lesions tend to ulcerate, is rarely encountered [3]. With its slightly different morphological presentation, it can pose a diagnostic dilemma, particularly in non-endemic areas. Because of the significant morbidity, it should be diagnosed and treated early. Rest and analgesics are usually helpful in mild cases [4]. Thalidomide is the drug of choice except in women of childbearing age. If started early, thalidomide brings down the severity very rapidly and also prevents its recurrence. For cases where it is contraindicated or where availability is a problem, systemic corticosteroid is the mainstay of treatment.

References

1. Sengupta U. Elimination of leprosy in India: an analysis. Indian J Dermatol Venereol Leprol. 2018;84:131–6.
2. Negera E, Walker SL, Bobosha K, Howe R, Aseffa A, Dockrell HM, Lockwood DN. T-cell regulation in erythema Nodosum Leprosum. PLoS Negl Trop Dis. 2017 Oct 9;11(10):e0006001.
3. Wankhade VH, Debnath P, Singh RP, Sawatkar G, Bhat DM. A retrospective study of the severe and uncommon variants of erythema nodosum leprosum at a tertiary health center in Central India. Int J Mycobacteriol. 2019;8:29–34.
4. Thangaraju P, Venkatesan S, Gurunthalingam M, Babu S. Rationale use of thalidomide in erythema nodosum leprosum-a non-systematic critical analysis of published case reports. Rev Soc Bras Med Trop. 2020;53:e20190454.

Chapter 25
Sudden Onset Painful Ulcers in an Adult Female

Gaurav Dash and Swetalina Pradhan

Abstract Type 2 lepra reaction (erythema nodosum leprosum) classically presents with recurrent crops of tender evanescent nodules and plaques associated with systemic manifestations. However, atypical morphological variants like bullous, pustular, ulcerated, hemorrhagic, and erythema multiforme-like ENL have been rarely reported. We are describing a 35-year-old female who presented with a history of painful inguinal lymphadenopathy followed by sudden onset of bullous and ulcerative lesions on acral parts with associated systemic symptoms following injectable drugs for inguinal lymphadenopathy. The patient was found to be a case of lepromatous leprosy with erythema nodosum leprosum in histopathology. The case posed diagnostic challenge to us because of the absence of obvious features of lepromatous leprosy and de novo presentation of ENL.

Keywords Inguinal tenderness · Ulcerative ENL · Erythema necroticans · Misdiagnosis · Drug reaction

Clinical Presentation

A 35-year-old female from Bihar presented to the dermatology OPD with painful ulceration over the extremities, face, and upper back for 7 days duration. The episode started with severe pain in the bilateral inguinal area leading to inability to walk 10 days back. For this, the patient consulted with local physicians and was prescribed various antibiotics (injectable and oral) and pain killers. After 2 days of medication, she noticed multiple erythematous plaques which subsequently developed vesiculation followed by ulceration within 1–2 days associated with fever and

G. Dash
Department of Dermatology, Hitech Medical College, Bhubaneswar, India

S. Pradhan (✉)
Department of Dermatology, AIIMS, Patna, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_25

joint pain. The patient was referred to dermatology with a diagnosis of drug reaction. Dermatological examination revealed multiple erythematous plaques with ulceration on surface of size around 0.5–2 cm distributed over the extensor aspect of the hands, legs, upper back, and left cheek (Figs. 25.1, 25.2 and 25.3). Mucosa, palm, and sole examination were normal. There were enlarged, tender bilateral inguinal lymph nodes. There was no history of prior drug intake, cough, cold, or diarrhea. Patient was also enquired about the history of leprosy due to her residence in an endemic area of leprosy. She had no history of epistaxis and nasal stuffiness, and also there was no history of leprosy in close contacts. There was no evidence of lepromatous leprosy on dermatological examination. However, peripheral nerve examination showed enlargement of bilateral common peroneal and left ulnar nerve

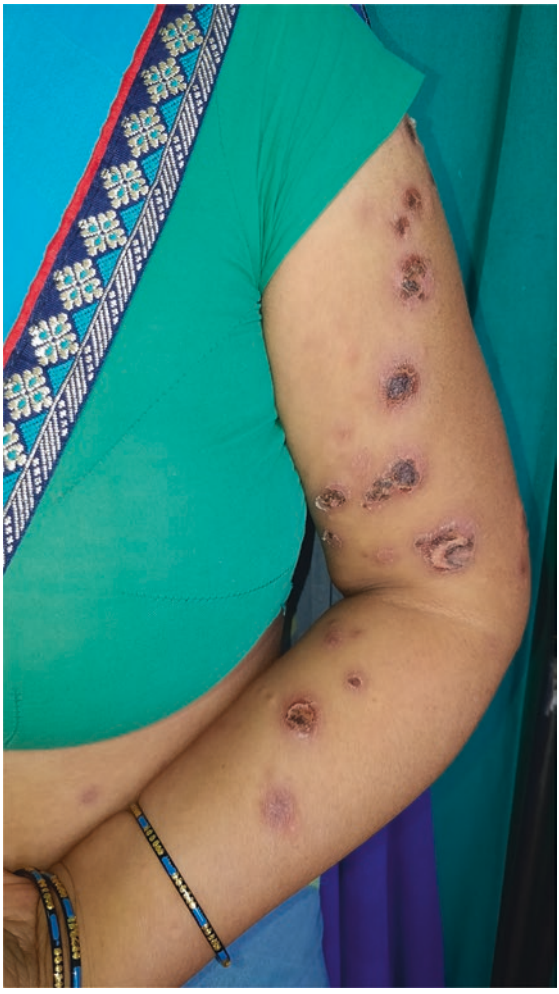

Fig. 25.1 Multiple erythematous plaques with ulceration on the surface of the size of around 1 cm covered with crust over the extensor aspect of the hands

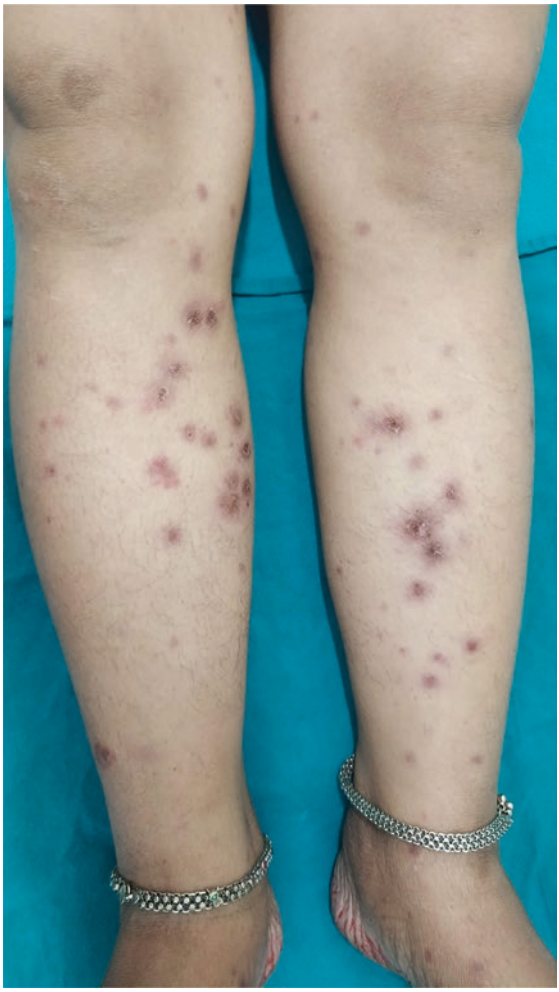

Fig. 25.2 Multiple erythematous plaques with ulceration on the surface of the size of around 0.5 cm over the extensor aspect of the legs with crusting at places

without any features of neuritis along with hypoesthesia on bilateral legs. There was no evidence of muscle weakness and visible deformity.

What Is Your Diagnosis?

1. Drug-induced bullous erythema multiforme.
2. Drug-induced bullous lupus erythematosus.
3. Bullous sweet syndrome.
4. Erythema nodosum leprosum.

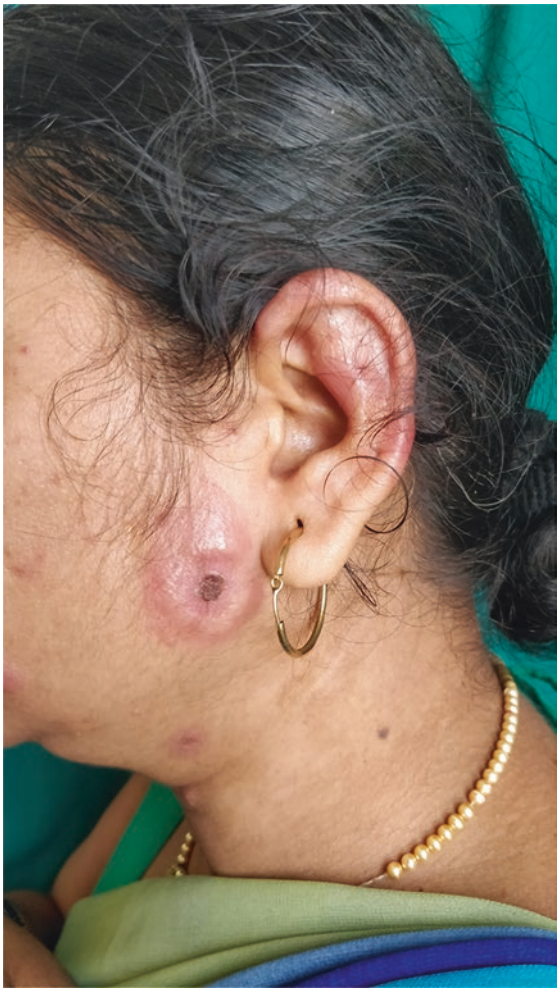

Fig. 25.3 Erythematous plaque with vesiculation and ulceration on the surface of the size of around 2 cm over the left cheek covered by crust

Investigation

- Routine investigations like complete blood count, liver function test, and renal function test were normal.
- Both ANA screening and ANA profile were negative.
- Fine needle aspiration cytology from the inguinal lymph nodes revealed inflammatory cells like lymphocytes, histiocytes, and epithelioid cell granuloma with positive ZN stain for *Mycobacterium leprae*.
- Slit skin smear for AFB revealed plenty of bacilli in globi (bacillary index 6+).

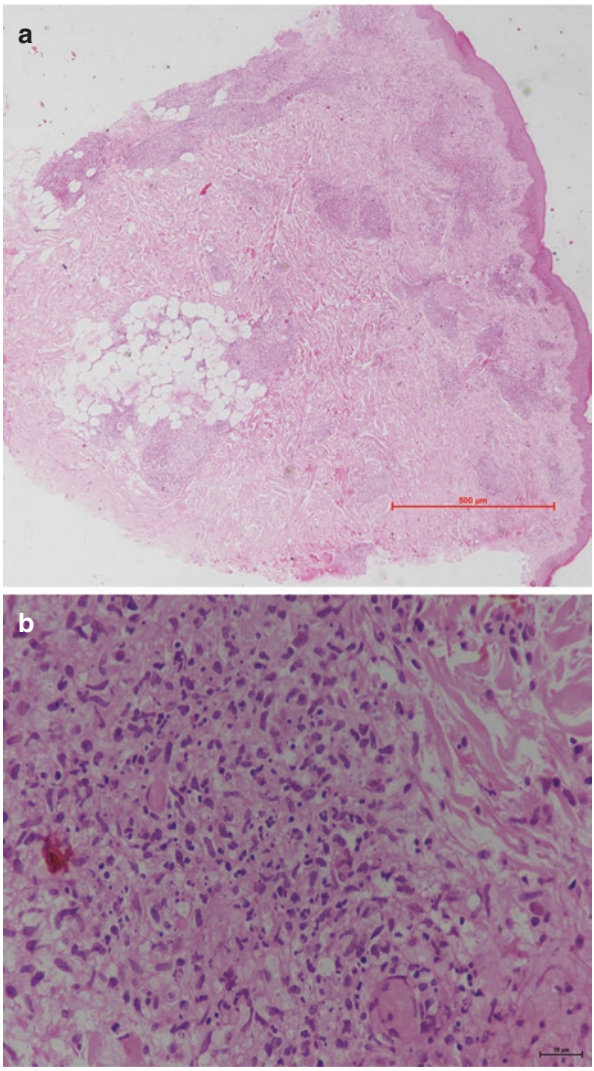

Fig. 25.4 (**a**) Scanner view H &E stain: Dense inflammatory cell infiltrate in dermis (**b**) 400X H&E stain: Perivascular, periadnexal mixed inflammatory cell infiltrates in the dermis consisting of lymphocytes, neutrophils, and plasma cells

- Histopathology revealed perivascular and periadnexal mixed inflammatory cell infiltrates in the dermis consisting of dense infiltration of neutrophils along with lymphocytes and plasma cells which was consistent with erythema nodosum leprosum with positive ZN stain for AFB (Fig. 25.4).

Final Diagnosis

Lepromatous leprosy with ulcerative erythema nodosum leprosum.

Discussion

Leprosy is a chronic granulomatous disorder involving the skin and nerves caused by *Mycobacterium leprae*. Lepromatous leprosy is one of the most severe variant of leprosy with a huge bacillary load. It is interrupted by episodes of erythematous edematous tender plaques and nodules (ENL) over extremities associated with systemic features called type 2 lepra reaction [1, 2]. The systemic manifestations due to immune complex-mediated damage include lymphadenitis, neuritis, iridocyclitis, arthritis, synovitis, myositis, epididymo-orchitis, glomerulonephritis, etc. [1] Various atypical cutaneous presentation of ENL like bullous, pustular, ulcerated, hemorrhagic, and erythema multiforme-like lesions are rarely described in the literature [1]. Ulcerative form of ENL or erythema necroticans rarely reported in the literature can pose a diagnostic challenge [3–5]. Ulcerative lesions in leprosy is indicative of severe ENL reaction in patients having very high bacillary load [4]. The causes of sudden painful ulcers in an adult female which were differentials in this case were drug-induced erythema multiforme, drug-induced bullous pemphigoid, bullous systemic lupus erythematosus, bullous sweet syndrome, and rarely ulcerative ENL.

Our case initially presented with severe pain in the inguinal area with fever for which she visited multiple physicians and was prescribed with various antibiotics (injectable and oral). Following which, there was development of multiple erythematous plaques over the extremities, face, and upper back which subsequently developed vesiculation followed by ulceration within 1–2 days along with associated fever and joint pain. It was misdiagnosed by physicians as a drug reaction to antibiotics. On the day of presentation, the patient also had tender enlarged inguinal lymph nodes. Our differential diagnosis were bullous SLE (looking at lesions over sun-exposed area with fever joint pain), drug-induced bullous erythema multiforme (looking at acral distribution and temporal correlation with antibiotics), bullous ENL (taking into account the sudden onset of erythematous, tender nodules, and plaques developing ulceration mostly over extremities and upper back with tender inguinal lymphadenopathy and systemic symptoms), and bullous sweet syndrome (looking into pseudo-vesicular look over the cheek with fever). Routine investigations like complete blood count and liver and renal function test were normal which ruled out bullous sweet syndrome. Antinuclear antibody was negative which ruled out bullous SLE. Fine needle aspiration cytology from inguinal lymph nodes revealed plenty of acid-fast bacilli in globi which clinched the diagnosis of bullous ENL which was later confirmed by histopathology study.

Mainstay of management in type 2 lepra reaction are corticosteroids and thalidomide [5]. Patient was started on multidrug therapy (MDT) for 12 months along with oral prednisolone 40 mg and thalidomide 400 mg and then gradually tapered after remission. Counseling was done regarding hand and foot care.

This case is being described in the view of a rare presentation of ENL and diagnostic dilemma because of a de novo presentation without any history of multidrug therapy.

References

1. Sethuraman G, Jeevan D, Srinivas CR, Ramu G. Bullous erythema nodosum leprosum (bullous type-2 reaction). Int J Dermatol. 2002;41:363–4.
2. Jopling WH. Reactions in leprosy (reactional states). In: Handbook of leprosy. London: William Heimann Medical; 1984. p. 68–77.
3. Sirka CS, Panda M, Pradhan S, Baisakh MR. Necrotic erythema Nodosum Leprosum healing with extensive scars. Indian Dermatol Online J. 2017;8:509–11.
4. Bala S, Sen S, Chatterjee G, Gangopadhyay A. Atypical erythema nodosum leprosum as the presenting feature in multibacillary leprosy: a case report. Indian J Dermatol. 2014;59:94–5.
5. Vashisht D, Das AL. Bullous erythema nodosum leprosum. Med J Armed Forces India. 2013;69:71.

Chapter 26
Multiple Annular Plaques

Ashmiya Razak and Manjunath Shenoy

Abstract A 38-year-old male patient presented with 2 months history of asymptomatic annular lesions on the back. Examination revealed multiple annular plaques with sloping margins were distributed asymmetrically over the back. Histopathology and skin smear for lepra bacilli aided the diagnosis. A final diagnosis of mid-borderline leprosy was confirmed.

Keywords Mid-borderline leprosy · Slit skin smear · Histopathology

Clinical Presentation

A 38-year-old male patient presented with asymptomatic annular lesion on the back for the past 2 months. He then noticed reddening and swelling of the skin over the lesions which were sudden in onset.

On examination, multiple well-defined annular plaques of varying sizes distributed over the back, punched-out inner margin with normal skin in the center, and a sloping outer edge ("Swiss cheese" appearance) were present (Fig. 26.1). Erythema and edema were noticed over the lesions. Tactile sensation was impaired over the skin lesions. Asymmetrical nerve thickening of the ulnar, common peroneal, and greater auricular nerves was also observed. There were no motor deficits.

A. Razak · M. Shenoy (✉)
Department of Dermatology, Venereology and Leprosy, Yenepoya Medical College, Mangalore, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_26

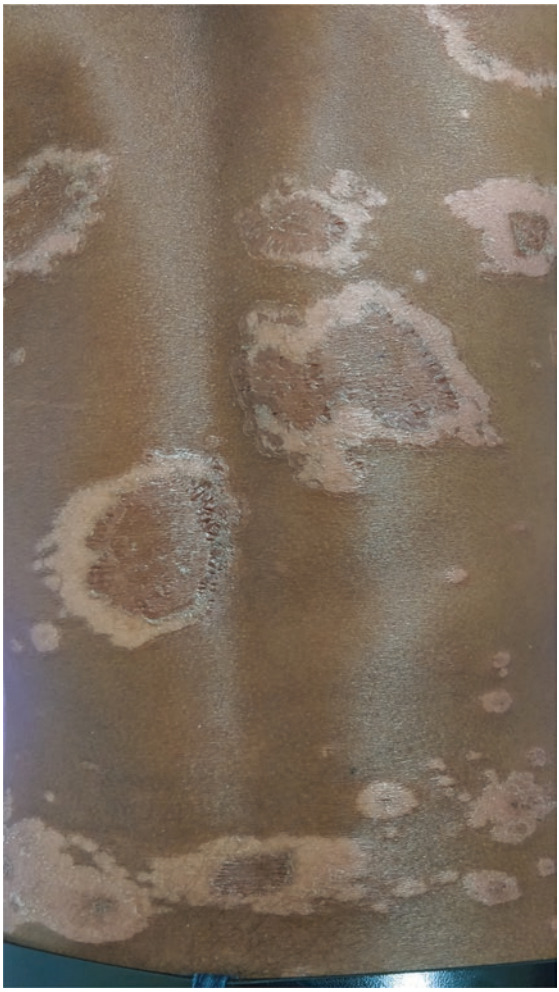

Fig. 26.1 Annular plaques with Swiss Cheese appearance lesions on the back

What Is Your Diagnosis?

1. Mid-borderline leprosy.
2. Sweet's syndrome.
3. Tinea corporis.

Investigations

- Routine investigations were within normal limits.
- Slit skin smears from the ear lobe and a lesion were positive for acid-fast bacilli with a bacteriological index of 2+ on the ear lobe. Skin biopsy from the lesion

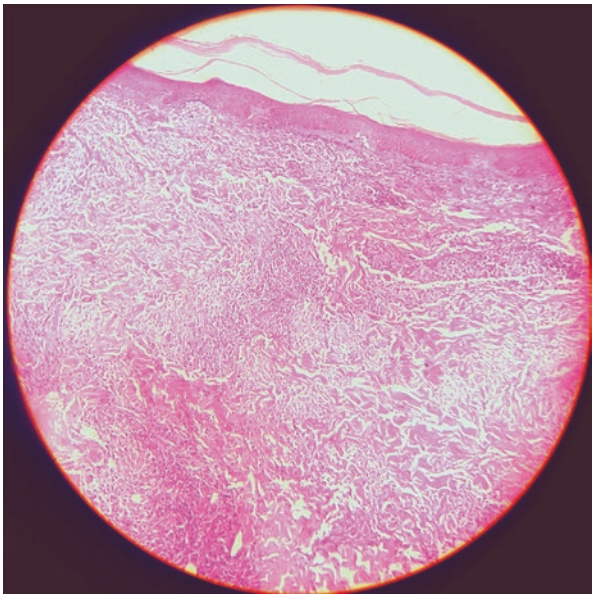

Fig. 26.2 Multiple curvilinear granulomas composed of histiocytes and epithelioid cells in the upper and mid-dermis (H&E × 100)

over the back showed multiple curvilinear granulomas composed of histiocytes and epithelioid cells in the upper and mid-dermis (Fig. 26.2).

Final Diagnosis

Mid-borderline leprosy in type 1 lepra reaction.

Discussion

Mid-borderline (BB) leprosy is the most unstable form of leprosy. Due to its immunological instability, this form of the disease is often short-lived. These patients may either upgrade to borderline tuberculoid type or more often downgrade to borderline lepromatous leprosy. The characteristic lesions seen here are annular plaque with punched-out inner edge and a sloping outer edge that merges with the normal skin. Normal-looking skin within the plaque gives a "Swiss cheese" appearance (or punched out) to the lesion [1]. Cutaneous and nerve lesions are multiple and have a tendency for asymmetry. Skin smear may be negative or may show low positivity from selective sites. Histopathologically, mid-borderline leprosy shows a combination of characteristics of both borderline tuberculoid and borderline lepromatous leprosy with a mixture of epithelioid cells and macrophages. Intracellular and extracellular edema within the granuloma and dermis is a common feature [2].

Type 1 reactions are typically seen among patients with an unstable immunological response. It is a type of delayed hypersensitivity reaction with a sudden alteration in the cell-mediated immunity of the patient. There is an increased cellular response to *M. leprae* antigens in the skin. They may occur in patients with borderline tuberculoid (BT), mid-borderline, and borderline lepromatous leprosy. They present as erythema and edema of existing skin lesions, eruption of fresh lesions, and inflamed nerves causing sensory and motor neuropathy [3].

Risk factors for the development of type 1 reactions are borderline group of patients, older age group, facial patch, and multiple patches with multiple nerve involvement. Treatment for type 1 reaction must be initiated promptly to prevent deformities. Various modalities of treatment are nonsteroidal anti-inflammatory drugs and systemic corticosteroids which is considered to be the drug of choice [4].

Our patient was initiated on MB-MDT and oral prednisolone, following which redness and swelling of lesions reduced considerably (Fig. 26.3).

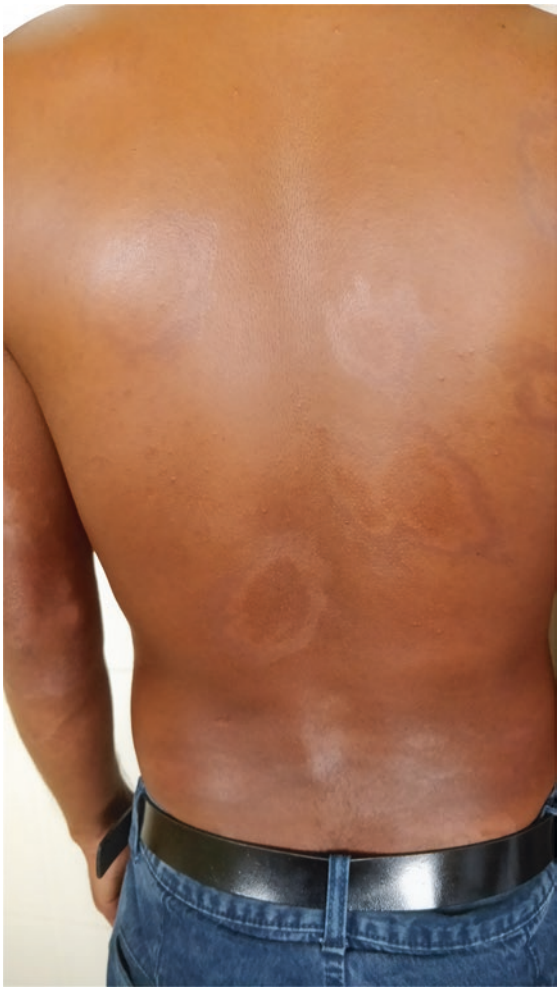

Fig. 26.3 Subsidence of erythema and edema on the plaques

References

1. Shenoy SM, Shenoy MM. Mid-borderline leprosy. Indian Dermatol Online J. 2013;4(2):162.
2. Lee DJ, Rea TH, Modlin RL. Leprosy. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, editors. Fitzpatrick's dermatology in general medicine, vol. 2. Philadelphia: McGraw-Hill; 2012. p. 2253–62.
3. Walker SL, Lockwood DN. The clinical and immunological features of leprosy. Br Med Bull. 2006;77-78:103–21.
4. Pandhi D, Chhabra N. New insights in the pathogenesis of type 1 and type 2 lepra reaction. Indian J Dermatol Venereol Leprol. 2013;79:739–49.

Chapter 27
Non-healing Ulcer on the Sole

Anugandha Ghatge and Bhushan Madke

Abstract Trophic ulcer or chronic plantar ulcer of leprosy is one of the primary causes of disability and deformity in the disease. Hereby, we are reporting a case of leprosy with trophic ulcer over the left foot. Managing trophic ulcers is difficult not only because of its recurrent and recalcitrant nature but also because the etiopathogenesis of the ulcer may be different in each case. A detailed clinical examination of the patient, vascular status, and ulcer is required to determine the etiology and plan the management accordingly.

Keywords Leprosy · Trophic ulcer · Plantar ulcer

Clinical Presentation

A 44-year-old male presented with a non-healing ulcer for 1 year over the forefoot of the left leg along with loss of sensation over bilateral lower limbs below the knees and hands for two years. He was diagnosed as a case of lepromatous leprosy six years back and completed his multibacillary multidrug therapy in the year 2016. He had no history of diabetes, hypertension, and other comorbidities. Nerve examination showed rope-like thickening of the bilateral ulnar and common peroneal nerve. Sensory-motor examination showed the presence of anesthesia in glove and stocking distribution and positive card test, book test, and pen test. On physical examination, he had madarosis and ichthyosis over bilateral lower limbs due to anhidrosis. Cutaneous findings showed a single ulcer of size 2 × 2 cm with raised margins and hypertrophic edges covered with slough, present over the ball of the great toe (first metatarsophalangeal joint) of the left foot as shown in Figs. 27.1 and 27.2.

A. Ghatge · B. Madke (✉)
Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Medical Sciences, Jawaharlal Nehru Medical College, Wardha, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_27

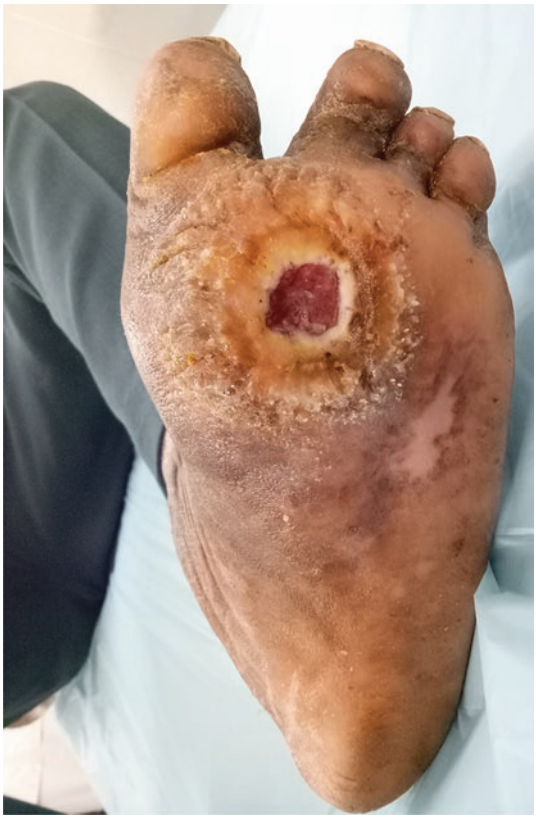

Fig. 27.1 Shows single ulcer of size 2 × 2 cm present over the ball of the great toe of the right foot

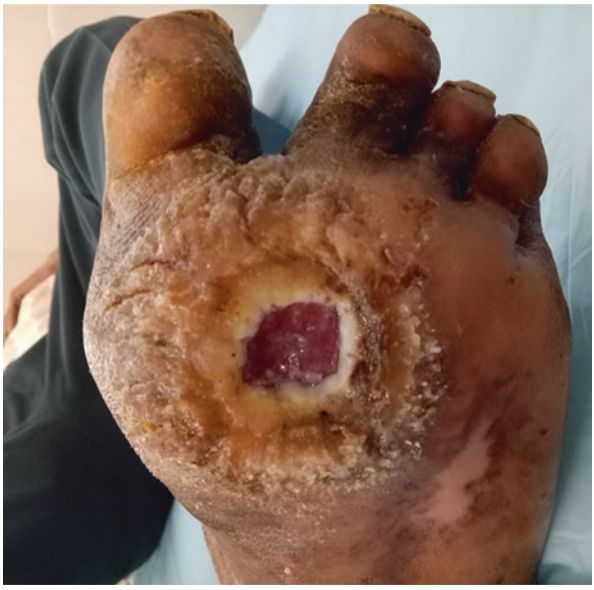

Fig. 27.2 Shows ulcer with raised margins and hypertrophic edges covered with slough

What Is Your Diagnosis?

1. Trophic ulcer in Hansen's disease.
2. Diabetic foot ulcer.
3. Venous ulcer.
4. Arterial ulcer.

Investigations

- All routine blood investigations were within normal limits.
- Arterial and venous color Doppler of the right lower extremity showed normal blood flow in both arterial and venous systems.
- Slit skin smear was performed after thorough clinical examination, which showed the bacteriological index of 4+.
- Skin biopsy was taken from anesthetic area which on histology showed a diffuse granulomatous reaction with macrophages, large foam [lepra] cells, and many intracellular bacilli frequently in spheroidal masses along with absence of epithelioid and giant cells.

Final Diagnosis

Lepromatous leprosy completed treatment with trophic ulcer without reaction.

Discussion

Leprosy is one of the most common causes of non-traumatic peripheral neuropathy in the whole world [1]. According to recent data released by NLEP in 2016, India has the highest burden of leprosy accounting for 60% of new cases reported globally every year and is also among the 22 "global priority countries" that contribute 95% of world numbers of leprosy [2]. Leprosy is a chronic infectious disease with variable morbidities which can present with skin lesions and nerve damage leading to loss of sensation and intrinsic muscle paralysis. This can lead to various deformities and disabilities like wrist drop, claw hand, foot drop, and trophic ulcers. Out of various disabilities of leprosy, plantar ulceration is most common and can be seen in 10% of leprosy patients [3].

The word "trophic" is derived from the Greek word "trophe" which means nutrition. Damage to the nerves during disease leads to sensory loss which in turn enhances the risk of trauma to the patient's feet leading to chronic plantar

ulceration. Various pathogenic mechanisms involved in the development of trophic ulcer are as follows [4]:

(a) Continuous pressure, causing necrosis due to lack of blood supply.
(b) Concentrated high pressure, causing cutting/crushing by mechanical violence.
(c) Heat/cold, causing burning or frostbite.
(d) Repetitive mechanical stress of moderate degree, causing inflammation and autolysis.
(e) Pressure on the infected tissue, resulting in spread of infection.

A trophic ulcer undergoes different stages before developing into an overt ulcer. These can be classified into three stages [3]:

- *Stage of threatened ulcer:* Pre-ulcerative stage of aseptic inflammation. Increased stress exerted over a period gives rise to a traumatic [aseptic] inflammation in the subcutaneous layer of the sole, which is most vulnerable to mechanical stress. This usually occurs under a joint or a bony prominence just distal to the head of a metatarsal. The affected site is edematous and often tender to deep digital pressure.
- *Stage of concealed ulcer:* In this stage, inflamed site undergoes necrosis due to the stress of continued walking, with the subcutaneous tissue undergoing necrosis. The liquefied tissue mixed with blood is forced to the surface by continued walking to present as a blister. This stage may go unnoticed. With the formation of the necrotic blister, the destruction of the subcutaneous tissue is complete, except that the "ulcer" is not seen or obvious because it is still covered with skin.
- *Stage of overt or open ulcer:* This is the stage when the skin overlying the blister breaks open and the necrotic area becomes exteriorized.

Trophic ulcers on the sole of the feet or fingertips usually develop at sites exposed to repetitive high pressures during activities of daily living like walking or working. Hence, the common sites of ulcerations on the sole of the foot are the weight-bearing areas like metatarsal heads in the forefoot, followed by heel and lateral border.

Clinical differentiation of various causes of plantar ulcers, i.e., arterial, venous, and neuropathic, is mentioned in Table 27.1.

Plantar ulcers are generally chronic, recurrent, and difficult to heal in nature. Management of such non-healing leg ulcers comprises primarily the treatment of the root cause along with local treatment methods, medications, or agents that altogether help in their reestablishment of the standard biological healing system. Here the patient was managed by using PRF (platelet-rich fibrin clot) and advised to wear microcellular rubber (MCR) footwear.

Various medical and surgical treatment modalities are tried in plantar ulceration such as collagen dressings, application of phenytoin, topical metronidazole, topical growth factors like PDGF, EGF, hyperbaric oxygen therapy [HBOT], vacuum-assisted closure [VAC], sesamoidectomy, subtotal metatarsectomy, etc. Recent studies have shown the usage of platelet-rich plasma (PRP) and platelet-rich fibrin

Table 27.1 Clinical differentiation of various causes of plantar ulcers

Assessment criteria	Venous ulcer	Arterial ulcer	Neuropathic ulcer
Pathophysiology	Valvular incompetence or venous outflow obstruction	Reduction in arterial blood flow leads to decreased perfusion of the tissues	Peripheral neuropathy leads to repetitive stress and injuries
Site	Gaiter region of the leg mainly medial aspect	Toes and distal parts of feet	Pressure-bearing areas like the metatarsal head or heels
Pain	Throbbing, aching, heavy feeling in the leg	Intermittent claudication, worse at night	Painless ulcers
Ulcer characteristics	Shallow with flat margins and granulated base	Small deep irregular ulcer with necrotic base. Cold limbs and absent pulses	Punched-out ulcer with callosities
Lower limb features	Dilated veins at the ankle, crusty hyperkeratotic skin. Pedal pulses present, ABI > 0.9	Skin feels cooler to touch, pallor on leg elevation, absent pedal pulses, ABI < 0.9	Dry and shiny skin. Loss of sensation with warm feet and good pulses

(PRF) clot in treatment of trophic ulcer which directly introduces various growth factors and cytokines, thereby normalizing the metabolic process, promoting neoangiogenesis, and activating local immunity [5]. Methods of prevention of trophic ulcer include:

1. Education.
2. Self-care procedures: inspection, soaking in water, scraping, oiling, and split.
3. Protective footwear: use of MCR footwear.

References

1. Pinheiro RO, de Souza SJ, Sarno EN, Sampaio EP. Mycobacterium leprae–host-cell interactions and genetic determinants in leprosy: an overview. Future Microbiol. 2011;6(2):217–30.
2. Rao PN, Suneetha S. Current situation of leprosy in India and its future implications. Indian Dermatol Online J. 2018;9(2):83–9.
3. Riyaz N, Sehgal VN. Leprosy: trophic skin ulcers. Skinmed. 2017;15(1):45–51.
4. Sabato S, Yosipovitch Z, Simkin A, Sheskin J. Plantar trophic ulcers in patients with leprosy: a correlative study of sensation, pressure and mobility. Int Orthop. 1982;6(3):203–8.
5. Anandan V, Jameela WA, Saraswathy P, Sarankumar S. Platelet rich plasma: efficacy in treating trophic ulcers in leprosy. J Clin Diagn Res JCDR. 2016;10(10):WC06–9.

Chapter 28
40-Year-Old Male with Claw Hand

Pooja Sahu and Bhushan Madke

Abstract Leprosy remains a leading cause of peripheral neuropathy and disability in the world. The disease is feared for the deformities and disability it produces in its host. Patients presenting with neuritis should be regularly monitored for nerve function impairment (NFI). For effective monitoring, assessments need to be carried out regularly on patients. The most important factor to prevent disability in leprosy patients is early detection and adequate treatment of neural impairment. We are discussing a case of borderline lepromatous leprosy who presented with claw hand.

Keywords Leprosy · Deformities · Neuritis

Clinical Presentation

A 40-year-old male noticed a few hypoaesthetic, hypopigmented patches on his upper extremities for two years along with tingling and numbness over the right hand. He reported difficulty in holding objects and doing fine movement. On further enquiry, there was a history of glove type of anaesthesia and decreased sensation over the palm which led to unnoticed injury. The right hand showed a complete claw hand deformity (Fig. 28.1) with flattening of the palm due to severe thenar and hypothenar atrophy, together with finger shortening and distal digital resorption. Sensory impairment was evaluated by examination of two-point discrimination, pin prick, and thermal testing which were impaired. He had ichthyosis over bilateral lower limbs due to anhidrosis. Froment's book test and Wartenberg's card tests were positive on the right hand. Uniform rope-like thickening of the right ulnar nerve was present.

P. Sahu · B. Madke (✉)
Department of Dermatology, Venereology and Leprosy, Datta Meghe Institute of Medical Sciences, Jawaharlal Nehru Medical College, Wardha, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_28

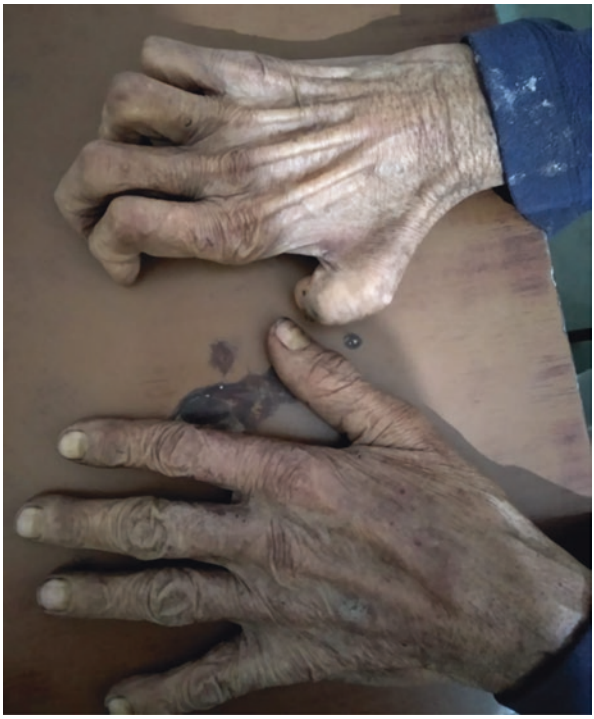

Fig. 28.1 Combined ulnar and median nerve paralysis (total claw hand) of the right hand

What Is Your Diagnosis?

- Leprosy.
- Cervical radiculopathy leprosy.
- Dupuytren's contracture.
- Klumpke's paralysis.
- Lower brachial plexopathy.
- Sclerodactyly.

Investigations

- Slit skin smear along with bacteriological index and morphological index.
- Skin biopsy taken from anaesthetic area showed a diffuse granulomatous reaction with macrophages, large foam cells, and many intracellular bacilli frequently in spheroidal masses along with the absence of epithelioid and giant cells.
- Nerve USG: Uniform cylindrical thickening of the right ulnar nerve.
- Nerve biopsy shows expanded nerve fascicle, with endoneurial infiltration by foamy macrophages (Fig. 28.2).
- Nerve conduction study showed reduced amplitude of sensory and motor nerve action potential.

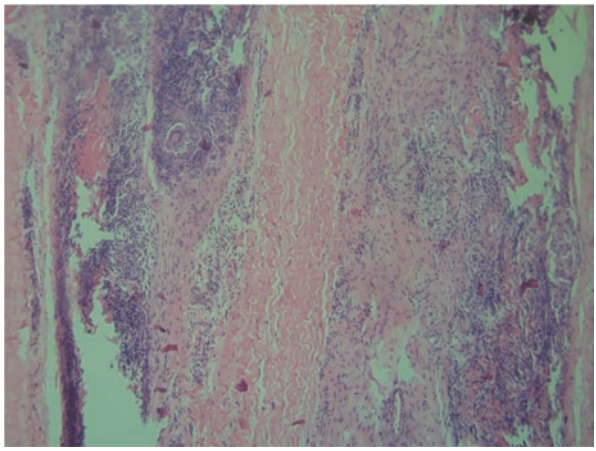

Fig. 28.2 Nerve biopsy shows expanded nerve fascicle, with endoneurial infiltration by foamy macrophages

Final Diagnosis

Borderline lepromatous leprosy with right claw hand.

Discussion

Deformities are seen in approximately 20–25% of leprosy patients, and common factors include type of leprosy (incidence higher in MB), the duration of active disease, and number of nerve trunks involved in the patient. Lepromatous and borderline types carry a much greater risk than tuberculoid and indeterminate types [1, 2]. In our case, due to late diagnosis and no proper treatment with MB MDT, it resulted in claw hand deformity.

Primary impairments include:

- Banana fingers (due to heavy infiltration).
- Reaction hand or frozen hand when the hand is involved in reactional states.
- Swan neck deformity (Fig. 28.3).
- Motor paralytic.
- Ulnar nerve: "clawing" of the little and ring fingers (Fig. 28.4) (middle and index fingers may be normal, mildly clawed, or fully clawed) [3].
- Flattening of the hypothenar eminence.
- Wasting of interosseous muscles forming characteristic depression over the dorsum of the hand "guttering sign".
- Straightening of the thumb at MCP joint so that the proximal phalanx and metacarpal are in a line (if flexor pollicis brevis is paralyzed).
- High median nerve paralysis only intrinsic muscles of hand paralyzed median leads to 'z' thumb deformity.

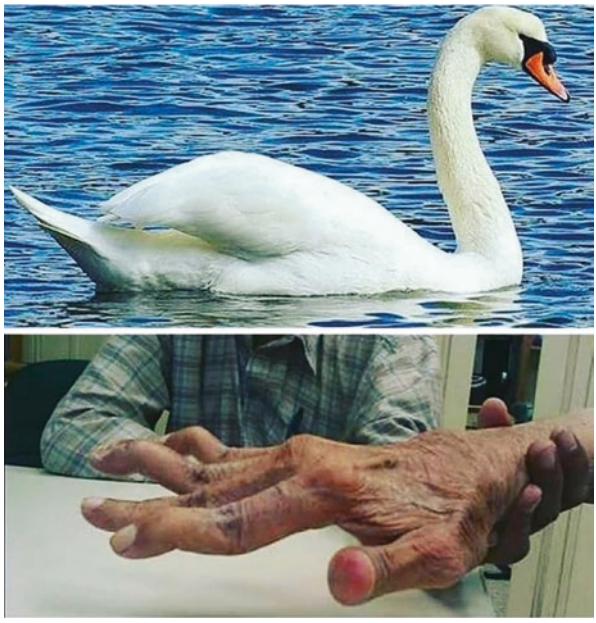

Fig. 28.3 Swan neck deformity showing hyperextension of the proximal interphalangeal joint and flexion of the distal interphalangeal joint

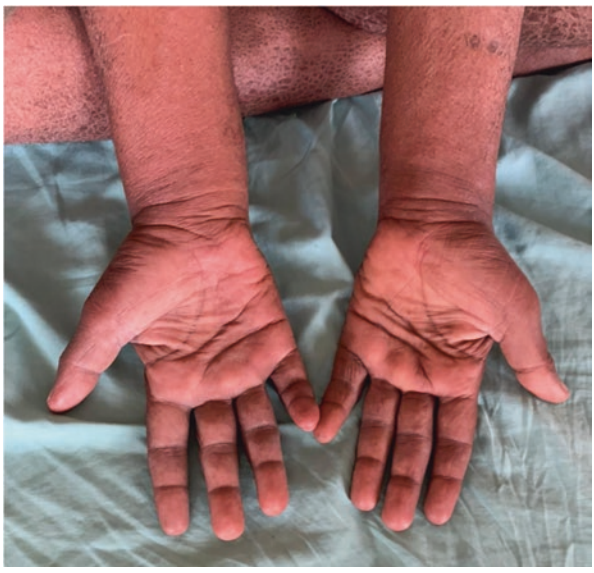

Fig. 28.4 "Clawing" of the little and ring fingers of the right hand

- Low median paralysis (intrinsic muscles of the hand paralyzed + muscles of the front of the forearm).
- Combined ulnar and median nerve paralysis (total claw hand)—ape thumb deformity (see Fig. 28.1).
- Triple paralysis (ulnar, median, and radial paralysis)—wrist drop.

Secondary deformities:

- Shortening of the fingers.
- Disorganization of the wrist.
- Mutilation of the hand and "straight stiff finger".

When a skin lesion overlies a nerve trunk, in a trauma-prone site, the terminal nerve fibres which are located superficially and easily compressible are damaged in leprosy. However, in our case, the probable cause for deformity was leprosy neuropathy since our patient was not diagnosed and treated in time as in leprosy early diagnosis is crucial because late recognition may lead the patient with some sequela of the disease.

Nerve damage is the most characteristic feature of the disease. The common clinical manifestations are due to sensory loss, followed by motor loss. Long nerves of the hands and feet are affected first, which get firm, hard, and fibrosed. In tuberculoid leprosy, nerve damage begins early and progresses rapidly by infiltration of the nerve by the granuloma. In lepromatous leprosy, peripheral nerve damage progresses slowly. Sensory nerve endings of the cooler parts of the body like the dorsum of the hands, feet, ears, and nose are affected as well [2].

Stages of nerve damage are stage of parasitisation, stage of host response, stage of clinical involvement, stage of nerve damage, and stage of nerve destruction [4].

Hand deformities severely affect quality of life and render patients occupationally non-productive. Patient's quality of life is hampered due to restricted daily routine activities and work to prevent further deterioration. Supportive treatment of deformity/disability includes exercise splints for neuritis, ulnar neuritis slab, median neuritis slab, cock-up slab for radial nerve, cylindrical splint for the interphalangeal joint thumb, and web spica/tuck S in splint functional slab for the hand. Home measures include using thick cloth or gloves for insulation for handling hot objects, tools with wooden or rubber-covered handles, grip aids, and splints to protect the hands [5]. Patient counselling is a vital component for social and occupational rehabilitation. Early detection of signs of nerve damage includes being aware to report numbness in the hand or foot, tingling sensation along the limbs, weakness in the hand, increase in areas of loss of sweating, increase in areas of impaired sensibility, increase in severity of a sensory loss, and increasing weakness of the hand muscles or paralysis.

In our patient, we first counselled him regarding all the precautionary measures. We provided him with grip aid and splints to ease his day-to-day activities. We also started him on first-line therapy MB MDT accompanied with a short tapering dose of prednisolone 0.5–1 mg/kg for the duration of 6 months, and regular physiotherapy exercises for occupational rehabilitation were advised.

References

1. Welsh RP, Hastings DE. Swan neck deformity in rheumatoid arthritis of the hand. Hand. 1977;9(2):109–16. https://doi.org/10.1016/s0072-968x(77)80003-x.
2. Srinivas G, Muthuvel T, Lal V, Vaikundanathan K, Schwienhorst-Stich EM, Kasang C. Risk of disability among adult leprosy cases and determinants of delay in diagnosis in five states of India: a case-control study. PLoS Negl Trop Dis. 2019;13(6):e0007495. https://doi.org/10.1371/journal.pntd.0007495.
3. Chan JP, Uong J, Nassiri N, Gupta R. Lessons from leprosy: peripheral neuropathies and deformities in chronic demyelinating diseases. J Hand Surg Am. 2019;44:411–15. https://doi.org/10.1016/j.jhsa.2018.07.007.
4. Job CK. Pathology and pathogenesis of leprous neuritis; a preventable and treatable complication. Int J Lepr Other Mycobact Dis. 2001 Jun;69(2 Suppl):S19–29.
5. Assis BPN, Lyon S, Grossi MA, Rocha MO. Risk factors for physical disability upon release from multidrug therapy in new cases of leprosy at a referral center in Brazil. Rev Inst Med Trop Sao Paulo. 2019;61:e13. https://doi.org/10.1590/s1678-9946201961013.

Chapter 29
A 55-Year-Old Male with Foot Drop and Claw Toes

Abhisek Mishra and Somen Kumar Pradhan

Abstract Leprosy, a disease caused by *Mycobacterium leprae*, is one of the major causes of preventable disability associated with peripheral neuropathy. Delayed diagnosis and poor monitoring of previously diagnosed patients are two of the major causes of deformities leading to disabilities. The combination of deformity and insensitivity involving lower extremities is responsible for severe functional limitations and formation of foot ulcers, increasing the risk of amputation. We are describing a case of borderline tuberculoid leprosy who presented with foot deformity after completion of anti-leprosy drugs.

Keywords Leprosy · Foot deformity · Disability

Clinical Presentation

A 55-year-old male patient farmer by occupation presented with a non-healing ulcer in his left foot for 6 months and clawing of the left second, third, fourth, and fifth toes and left foot drop for 8 years duration. The patient gave a history of hypopigmented patches over his left hand and left foot 10 years ago, for which he had taken WHO MDT for 2 years following which the skin lesions improved gradually over time. After completion of MDT, the patient developed left foot drop followed by clawing of his left toes (Fig. 29.1). He had no history of diabetes, hypertension, and other comorbidities. There was no family history of similar disease. Dermatological examination revealed relative loss of hair over the left forearm and left leg along with a burn scar on the left hand. On sensory examination, there was complete anaesthesia over the left foot (both dorsal and plantar aspect till ankle) along with loss of sensation over the left forearm and palm. Motor examination revealed flattening of thenar and hypothenar eminence, with guttering over the left hand (Fig. 29.2). There was a complete claw hand with positive Froment's sign and card

A. Mishra (✉) · S. K. Pradhan
Department of Community Medicine and Family Medicine, AIIMS, Bhubaneswar, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_29

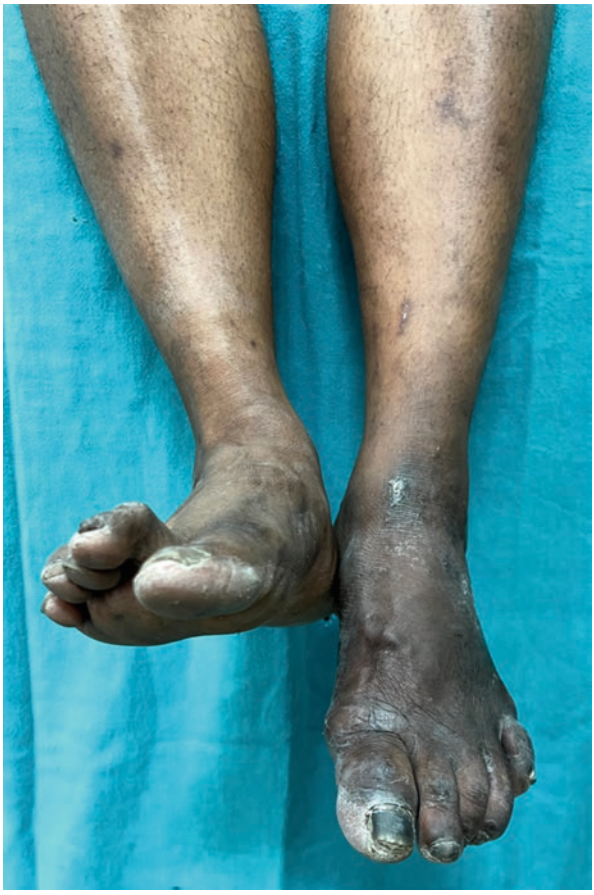

Fig. 29.1 Left foot drop with claw toes

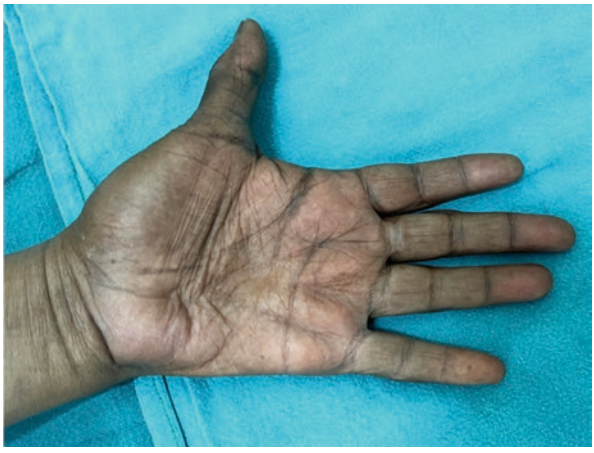

Fig. 29.2 Flattening of thenar and hypothenar eminences with guttering in the left hand

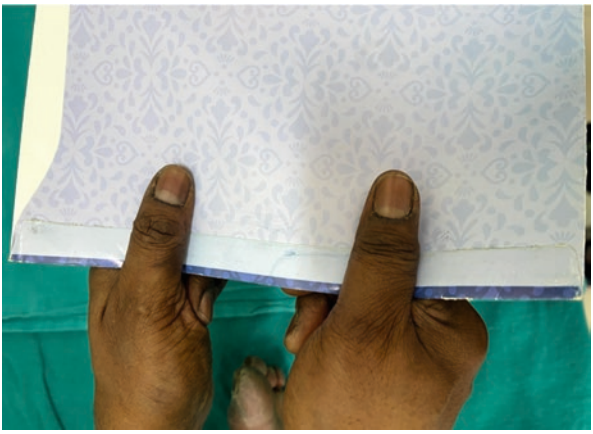

Fig. 29.3 Card test with positive Froment's sign

test on the left hand (Fig. 29.3). In addition, there was an ulcer on the forefoot behind the third toe of size 0.5 × 1 cm, oval in shape, surrounded by hyperkeratotic margin. Nerve examination showed thickening of the bilateral ulnar (left > right), bilateral radial cutaneous, left marginal mandibular branch of the facial nerve, and left common peroneal nerve.

What Is Your Diagnosis?

- Borderline tuberculoid Hansen's disease with hand and foot deformity.
- Diabetic neuropathy with hand and foot deformity.
- Sarcoidosis with hand and foot deformity.
- Compressive neuropathy with hand and foot deformity.

Investigations

1. Routine haematological examination, fasting blood sugar, and serum angiotensin-converting enzyme (ACE) level were within normal limits. Chest X-ray was normal.
2. Slit skin smear for AFB: negative.
3. Histopathology from the left forearm: nonspecific findings.
4. Nerve conduction test: nerve conduction study showed decreased amplitude of the sensory and motor nerve action potential.

Final Diagnosis

RFT case of borderline tuberculoid Hansen's disease with claw hand, claw toes, foot drop, and trophic ulcer.

Discussion

The present case came with a complaint of non-healing foot ulcer, foot drop, and clawing of toes in the left foot. He gave a history of hypopigmented patches over his left hand and left foot 10 years ago which was later diagnosed as leprosy. As per the patient, he has completed MDT after being diagnosed with the disease. After completion of MDT, the patient developed left foot drop followed by clawing of his left toes which could be due to silent neuropathy. There was a complete claw hand with a positive Froment's sign and card test on the left hand. The patient had left foot drop with fixed flexion deformity of the second, third, fourth, and fifth toes. This indicates involvement of the median nerve, ulnar nerve, common peroneal nerve, and posterior tibial nerve of left side extremities leading to grade 2 disability (Table 29.1) [2]. Some neuropathies having similar clinical pattern of those with leprosy are diabetic and amyloid neuropathy. However, deep tendon reflexes are usually preserved in leprosy contrast to these two conditions. Similarly, the involvement of nerves are diffuse, symmetrical in diabetic neuropathy as compared to focal, asymmetric nerve involvement in leprosy.[3]Our patient was not diabetic and had skin lesions of borderline tuberculoid leprosy apart from the deformities with asymmetrical nerve enlargement. The patient completed the PB MDT and later on developed deformities, which could be due to ongoing silent neuropathy or acute neuritis.

Usually, *M. leprae* bacilli enter the human body through the respiratory system. After entering the body, bacilli migrate towards the nervous tissue and infiltrate Schwann cells of nerve trunks leading to a subacute, demyelinating- and non-remitting-type neuritis. Invasion of Schwann cells and axons by *Mycobacterium leprae* leads to demyelination and axonal degeneration. This causes defective

Table 29.1 Peripheral nerve involvement in leprosy [1]

Nerve	Motor loss	Sensory loss
Ulnar nerve	Clawing of the ring and little fingers, loss of intrinsic muscle function	Anaesthesia over the medial two fingers of the hand
Median nerve	Loss of thumb opposition and grasp	Anaesthesia over the thumb
Radial nerve	Wrist drop	Anaesthesia of first web space
Common peroneal nerve	Foot drop	Anaesthesia over the lateral malleolus
Posterior tibial	Clawing of toes	Anaesthesia of the sole of the foot

regenerating response within nervous tissues, primarily involving cutaneous nerves and larger peripheral nerve trunks [4]. At this point, it is essential to diagnose silent neuropathy, which is characterized by sensory or motor impairment without skin signs of reversal reaction or erythema nodosum leprosum (ENL) and without evident nerve tenderness, spontaneous nerve pain, paraesthesia, or numbness [5]. Deformities are produced by nerve trunk damage indirectly through sensory loss and loss of motor power. Loss of sensation increases the vulnerability to injury and infections, leading to ulcers in the palm and sole. On the other hand, loss of motor power causes muscular imbalance leading to deformity and disability. Secondary to these deformities, because of altered position and dynamics, other musculoskeletal complications like joint contractures, adaptive shortening of muscles, and ulceration at dependent bony prominences follow [6].

As mentioned in the case details, there was a foot ulcer behind the left third toe of size 0.5 × 1 cm, oval in shape, surrounded by hyperkeratotic margin. Most common causes of trophic ulcers among leprosy patients are trauma, dry skin, animal or insect bite, and secondary infection on macerated skin. The common sites of ulcerations on the sole of the foot are the weight-bearing areas like metatarsal heads in the forefoot, followed by the heel and lateral border. While walking, pressure on insensitive feet is normally countered by contraction of intrinsic muscles of the feet which elevate the metatarsophalangeal (MTP) joint region upwards and forwards. When the posterior tibial nerve is affected due to neuropathy, this mechanism is hampered due to paralysis of small muscles. Furthermore, bowing at MTP joints results in increased pressure at localized areas causing local ischemia, inflammation, and breakdown of subcutaneous fat underneath the MTP joints. This leads to trophic ulcer in leprosy patients. It has a typical punched-out margin, which is thickened as a result of the body's protective response to further weight bearing and continued walking on the painless foot[7]. The management of this patient would be focussed on four steps:

1. *Treatment of trophic ulcer:* All simple ulcers will heal, if given sufficient rest, proper hygiene, and protection along with an aseptic wound environment. In addition to this, self-care plays an important role in ulcer healing. However, deep ulcers are less likely to respond to conservative treatment and will need surgical debridement, followed by dressing, and in a case of non-healing ulcer, skin replacement with graft or flaps will be required. Surgery is required mainly to remove a septic focus, to open up any tracks, and to remove any dead bone. Sometimes, in cases of recurrent ulceration of the forefoot, metatarsectomy is needed, while for a heel ulcer, some flap surgical procedures may be performed [1, 6].
2. *Correction and rehabilitation of claw hand, claw toes, and foot drop* (Table 29.2) [8].
3. *Prevention of further complications* [9].

    - Adherence to self-care practices.
    - Use of Micro Cellular Rubber (MCR) footwear.
    - Physiotherapy.

Table 29.2 Correction and rehabilitation of deformities

	Claw hand	Claw toes	Foot drop
Strengthening exercise	• Straighten the weak thumb and keep it straight for a few seconds. Hold the weak thumb steady with the other hand • Straighten the paralysed thumb using the other hand. Hold the base of thumb with the other hand and draw it away towards the palm	• Straighten the weak toes and hold it straight for a few seconds. Use the other hand to hold the weak toe steady • Straighten the paralysed toe using the other hand. Hold the base of thumb with the other hand and draw it away towards the palm	• Bend your foot up and hold it there for a few seconds • Practice it with the leg straight. Pull the foot up using a towel or strap • Repeat this movement several times
Instruments for physical aid	• Splints for prevention of deterioration and render the hands fit for reconstruction • Grip aids for activities of daily living in advanced cases of deformities	• Splints for prevention of deterioration and render the foots fit for reconstruction • Ankle-foot orthosis	• Splints for prevention of deterioration and render the foots fit for reconstruction • Ankle-foot orthosis
Reconstructive surgery	*Indications for RCS* • Patient should have completed full course of MDT • Reaction-free status for at least last 6 months • Steroid-free status for at least last 3 months • No intercurrent infection • There should not be any severe contractures/stiff joints If the patient has recent nerve function loss, he should be started on a course of steroids		

4. *Social rehabilitation* [10].

- Patients can be referred to a non-governmental organization or peer groups for adherence towards self-care management and for receiving psychosocial support.
- Affected persons can be linked to disability support and social welfare assistance schemes.

In our patient, who is a farmer by occupation, hand and foot deformity has severely affected his quality of life by preventing him from performing his daily activities independently. In addition to this, it has kept him out of his farming occupation making him vulnerable to poverty and leading to social insecurities. We advised him with appropriate grip aid, splints, and physiotherapy exercises in consultation with physical medicine and rehabilitation experts. A 6-month course of prednisolone 0.5–1 mg/kg dose was prescribed.

Lack of knowledge regarding foot care practices has led to a foot ulcer in the patient. For this, the patient was counselled on self-care practices to prevent foot ulcer and was provided a self-care kit containing scrapper, antiseptic solution,

moisturizing cream, gauze pieces, and a set of protective foot wear. The patient was also guided by a medical social worker regarding occupational rehabilitation and other social support schemes meant for persons with disability.

References

1. Moonot P, Ashwood N, Lockwood D. Orthopaedic complications of leprosy. J Bone Jt Surg–Ser B. 2005;87(10):1328–32.
2. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five-group system. Int J Lepr Other Mycobact Dis. 1966;34(3):255–73.
3. Nascimento OJM. Leprosy neuropathy: clinical presentations. Arq Neuropsiquiatr. 2013;71(9B):661–6.
4. Bhat RM, Prakash C. Leprosy: an overview of pathophysiology. Interdiscip Perspect Infect Dis. 2012;2012:181089.
5. Sehgal VN, Sardana K, Dogra S. Management of complications following leprosy: an evolving scenario. J Dermatolog Treat. 2007;18(6):366–74.
6. Virmond M. Indications for surgery in leprosy. Lepr Rev. 1998;69(3):297–304.
7. Atul Shah NS. IAL textbook of leprosy. In: Bhushan Kumar HKK, editor. IAL textbook of leprosy. 2nd ed; 2017. p. 526–7.
8. Directorate General of Health Services, Ministry of Health and Family Welfare. Government of India. Training Manual for Medical Officers. National Leprosy Eradication Programme. 2019. p. 262.
9. Central Leprosy Division M. Disability Prevention & Medical Rehabilitation; Guidelines for Primary, Secondary and Tertiary Level Care [Internet]. 2012. http://clinicalestablishments.gov.in/WriteReadData/516.pdf
10. World Health Organization. Towards zero leprosy Towards zero leprosy–Global Leprosy (Hansen's disease) Strategy 2021–2030. 2021. pp. 1–30. https://www.who.int/publications/i/item/9789290228509

Chapter 30
A 60-Year-Old Female with Corneal Opacity

Suvesh Singh and Swetalina Pradhan

Abstract Leprosy bacilli affect the eye through direct invasion, secondary to cranial nerve invasion or contiguous structures and inflammatory reaction. It commonly affects the anterior segment of the eye because it is cooler and rich in unmyelinated nerves. Facial nerve involvement led to paralytic lagophthalmos, exposure keratitis, and neurotrophic keratitis. Acute iridocyclitis and scleritis occur in type 2 reaction of lepromatous leprosy. Leprosy is termed "potential sight-threatening" and can lead to blindness secondary to lagophthalmos, uveitis, exposure keratitis, and cataract. The risk of ocular complication increases with the duration of disease despite treatment with MB-MDT. So early diagnosis can prevent visual complications in leprosy. We presented a case of lepromatous leprosy with recurrent episodes of ENL in the past and now present to us with left corneal opacity.

Keywords Leprosy · Lagophthalmos · Keratitis · Scleritis · Uveitis · Blindness

Clinical Presentation

A 60-year-old female from Saran, Bihar, was diagnosed with lepromatous leprosy with recurrent episodes of ENL and grade 2 disability since 4 years. She completed her MB-MDT treatment for 12 months in last year. Now she complained of dryness of the eye, decreased vision in the left eye, and inability to close her left eye for the past 8 months. History of occasional redness of the eye along with pain occurred during fever and crops of nodular eruption in the past. On eye evaluation, she had madarosis, trichiasis, and drooping of the upper eyelid with a gross defect in visual acuity (counting fingers at 5 m) in the left eye. There was no discharge from the eye, and she had normal ocular pressure. Schirmer's test showed dryness of the eye. Corneal opacity was present in the center of the left eye extending towards the limbus along with thickening and beading of the corneal nerve and decreased sensation

S. Singh · S. Pradhan (✉)
Department of Dermatology, Venereology and Leprosy, AIIMS, Patna, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_30

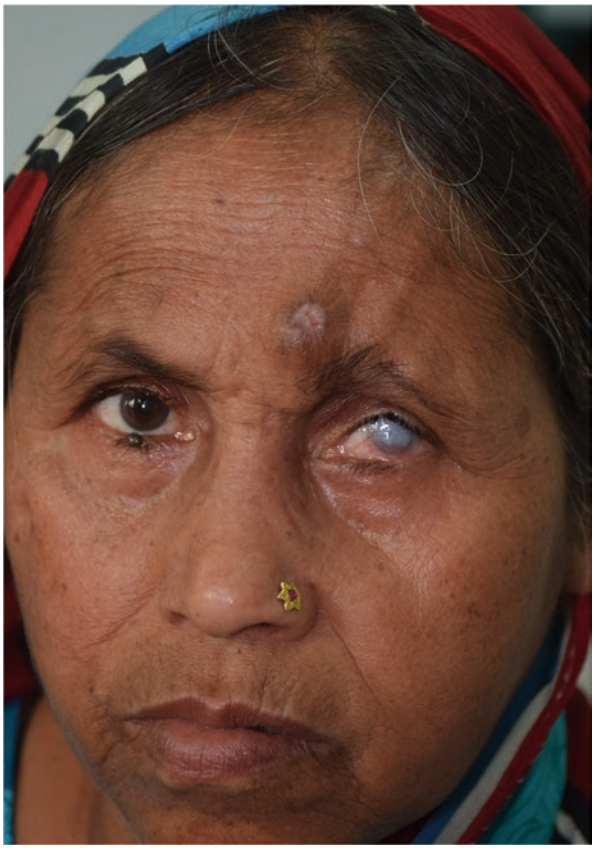

Fig. 30.1 Corneal opacity of the left eye

using the Cochet and Bonnet esthesiometer (Fig. 30.1). There was no feature acute iridocyclitis, iris pearls, calcification, muscle atrophy, festooning of the pupil, and synechia on slit-lamp examination. The lens in both eyes had a cataract. Sclera had no changes like thinning, ectasia, and staphyloma of globe perforation. The nasolacrimal duct was patent. She had ulnar, radial cutaneous, and common femoral nerve thickened along with ulnar clawing of the hand.

What Is Your Diagnosis?

- Leprosy.
- Sarcoidosis.
- Leishmaniasis.

Investigations

- Slit skin smear along with bacteriological index and morphological index.
- Skin biopsy taken from the aesthetic area showed a diffuse granulomatous reaction with macrophages, large foam cells, and many intracellular bacilli frequently in spheroidal masses along with the absence of epithelioid and giant cells. No LD bodies and culture on NNN media.
- Serum ACE level was normal.
- Nerve USG: Uniform cylindrical thickening of the right ulnar nerve.
- Slit-lamp examination, corneal sensitivity by using Cochet and Bonnet esthesiometer, Schirmer's test, and Goldmann applanation tonometry.
- Nerve conduction study showed reduced amplitude of sensory and motor nerve action potential.

Final Diagnosis

Lepromatous leprosy not in reaction with grade 2 disability, corneal opacity, and facial palsy.

Discussion

Eye complication in leprosy is directly proportional to the duration of disease, treatment status of the patients, facial patch, advancement of the disease, deformity, and disability of limbs [1, 2]. Early studies had reported incidence of eye complications ranging from 6 to 100% depending on the racial variation, and 3% had blindness and 11% had potentially sight-threatening ocular manifestations (PSOM), which includes cataract (65%), lagophthalmos (12%), reduced corneal sensation, corneal opacity (13%), iridocyclitis/uveitis (9%), scleritis, glaucoma, and dry eye syndrome [3]. The eye complication incidence has drastically reduced with the advent of MB-MDT treatment, and nowadays, most eye problems are due to the normal aging process. However, there is evidence that about 20% of multibacillary patients develop eye complications during treatment or within 5 years after treatment because of ongoing immune reactions and the slow evolution of preexisting nerve damage. Eye complications are seen predominantly in lepromatous followed by borderline and rarely in the tuberculoid pole of leprosy [4].

In our case, diagnosis of leprosy was based on clinical presentation, histological, and slit skin smear. In our case, eye complications developed due to late diagnosis

and recurrent episodes of ENL with iridocyclitis in the past, and late initiation of treatment with MB-MDT resulted in facial palsy, lagophthalmos, and exposure keratitis with left corneal opacity. Cataracts could be secondary to iridocyclitis and aging process. Hence, early diagnosis and treatment of leprosy are crucial.

Clinical Manifestation of Eye Involvement in Leprosy [5–8].

- *Ocular adnexa*: Madarosis(m/c), poliosis, trichiasis, ectropion, entropion, and lagophthalmos. Except for lagophthalmos, other features are more common in the lepromatous pole.
- *Cornea*: Superficial punctate keratitis (m/c), sub-epithelial keratitis, interstitial keratitis, pannus, thickening of corneal nerves, reduced corneal sensation, keratic precipitates, corneal ulcer, and corneal opacities. Corneal involvement can be primary or secondary (lagophthalmos is most common) and is the frequent cause of visual impairment in leprosy. Interstitial keratitis, pannus, and healed interstitial keratitis leaving corneal opacities are the most important primary corneal lesions which lead to visual impairment.
- *Sclera*: Episcleritis (more commonly seen in type 2 reaction) and scleritis. Long-standing scleritis can lead to scleral thinning, scleral ectasia, and staphyloma.
- *Iris*: Iris pearls, anterior synechia, posterior synechia, and festooned pupil, in advance cases, can complicate with uveitis, glaucoma, and iris nerve and smooth muscle atrophy due to post sympathetic ganglion denervation of an eye.
- *Ciliary body*: Premature presbyopia and phthisis bulbi.
- *Lens*: Cataract is due to normal aging process or uveitis or steroid therapy.
- *Retina*: Decrease contrast sensitivity leading to a frequent history of falls.
- *Lacrimal and nasolacrimal duct*: Decreased tear secretion, blockage of the duct, and chronic dacryocystitis.

In all leprosy patients, a simple eye examination with a flashlight in a dark room is sufficient to diagnose and should be done at every visit. The complete eye examination includes the following checklist: visual acuity, close eyes, lacrimal duct patency, corneal sensation, fluorescein use, pupil examination, and intraocular pressure.

Lagophthalmos occurs due to involvement of the zygomatic branch of the facial nerve, and early treatment with prednisolone therapy can prevent further eye complications. Treatment is dependent on the duration, width of the eyelid gap, exposure to the cornea, and presence or absence of corneal hypoesthesia. In case of long-standing lagophthalmos (>6 months), a gap of eyelid more than 2 mm on forced closer imminent corneal damage or ulcer and corneal drying leading to excessive dryness and redness indicates reconstructive surgical procedures like tendon transfer surgery, lid tightening procedures, and procedures for narrowing the palpebral fissure like tarsorrhaphy or lid-loading. Through a simple procedure, lateral tarsorrhaphy often shows an unsatisfactory outcome in terms of eye closure. Surgery is the only curative option for cataracts, but if caused secondary to uveitis, then treat with a steroid prior till the eye is quiet [7].

A corneal ulcer occurs due to microbial infection, which results in corneal opacity. The risk factors for corneal opacity are lagophthalmos, nasolacrimal duct

infection, reduced corneal sensation, nasolacrimal duct infection, and hand infection. A corneal ulcer is a medical emergency and should be managed by an ophthalmologist, and corneal scraping should be sent for culture and sensitivity, although treatment should be started immediately. Topical broad-spectrum antibiotics like fluoroquinolones and aminoglycosides are the mainstay of treatment. In case of non-healing ulcer caused due to fungal infection, it should be treated with the antifungal drug [7].

In our case, the patient was already treated with MB-MDT, and her current concern is the hand deformity and visual defect. The first step in management of eye complication in our case was to counsel her regarding all the precautionary measures. We explained the habit of blinking regularly with a voluntary, conscious effort, i.e., "think and blink" and close the eyes with an effort from time to time. The eyes can be protected with spectacles or a shield while moving out in the open, sun exposure and a pad or head cloth while sleeping. The eyes should be washed with clean water twice daily and mopped gently with a clean cloth. The patient was referred to an ophthalmologist for coreoplasty, temporalis muscle tendon transfer, and later for cataract surgery. Hand grip aid and splint for clawing of hand (see our previous chapter on hand deformity in leprosy) were advised along with regular physiotherapy for occupational rehabilitation.

References

1. Lamba PA, Kumar DS. Ocular involvement from leprosy. Indian J Opthalmol. 1984;32:61–3.
2. Lamba PA, Rohatgi J, Bose S. Factors influencing corneal involvement in leprosy. Int J Lepr Other Mycobact Dis. 1987 Dec;55(4):667–71.
3. Junaid SW, Saiba Rashid MS. Ocular manifestations in leprosy–a clinical study. JK Pract. 2005;12(1):14–7.
4. Monteiro LG, Campos WR, Orefice F, et al. Study of ocular changes in leprosy patients. Indian J Lepr. 1998;70:197–202.
5. Parikh R, Thomas S, Muliyil J, et al. Ocular manifestation in treated multibacillary Hansen's disease. Ophthalmology. 2009 Nov;116:2051–7.e1.
6. Reddy GN, Reddy GA. Ocular manifestations of leprosy. Trop J Ophthalmol Otolaryngol. 2019;4:414–8.
7. Bairappagari MEJ, Thompson KJ, Daniel E. The eye in leprosy, chapter 3.1. In Scollard DM, Gillis TP, editors. International textbook of leprosy. 5 January 2017, posting date. www.internationaltextbookofleprosy.org
8. Sekhar GC, Vance G, Otton S, et al. Ocular manifestations of Hansen's disease. Doc Ophthalmol. 1994;87(3):211–21.

Chapter 31
Reticulate Purpura and Painful Ulcers

Shirin Bakshi and Tarun Narang

Abstract Lucio leprosy (LuLp) is a diffuse, non-nodular form of leprosy that is primarily seen in Mexico and Central America with a few cases being reported from Southeast Asian countries and South American, the Pacific, Middle East, and African nations. Lucio phenomenon (LP) is a reactional state that is characteristically associated with LuLp. There are only a handful of reports of LP from India and it is at times difficult to differentiate it from necrotic erythema nodosum leprosum. We are describing a 35-year-old female who had both Lucio leprosy and Lucio phenomenon.

Keywords Lucio leprosy · Lucio phenomenon

Clinical Presentation

A 35-year-old female with no known comorbidities presented with multiple painful ulcers over the trunk and upper and lower limbs since the past 2–3 months. There was no history of fever or any other constitutional symptoms. On further probing, a positive history of hypoesthesia over both upper and lower limbs, spontaneous blistering, and epistaxis could be elicited. General examination revealed pallor, lymphadenopathy (inguinal and axillary), and bilateral pedal edema. Mucocutaneous examination revealed madarosis; diffuse infiltration of the skin of the face, ear lobes, and trunk; asymmetrical thickening of multiple peripheral nerves; as well as glove and stocking pattern of sensory impairment, in addition to bilateral, tender, discrete, mobile, inguinal lymphadenopathy. Cutaneous examination revealed multiple, coalescing, sharply angulated ulcers with jagged margins and necrotic center in addition to overlying tender, erythematous nodulo-plaques on the face, trunk, and extremities (Fig. 31.1a–d). The rest of the systemic examination was non-contributory.

S. Bakshi · T. Narang (✉)
Department of Dermatology, Venereology and Leprology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_31

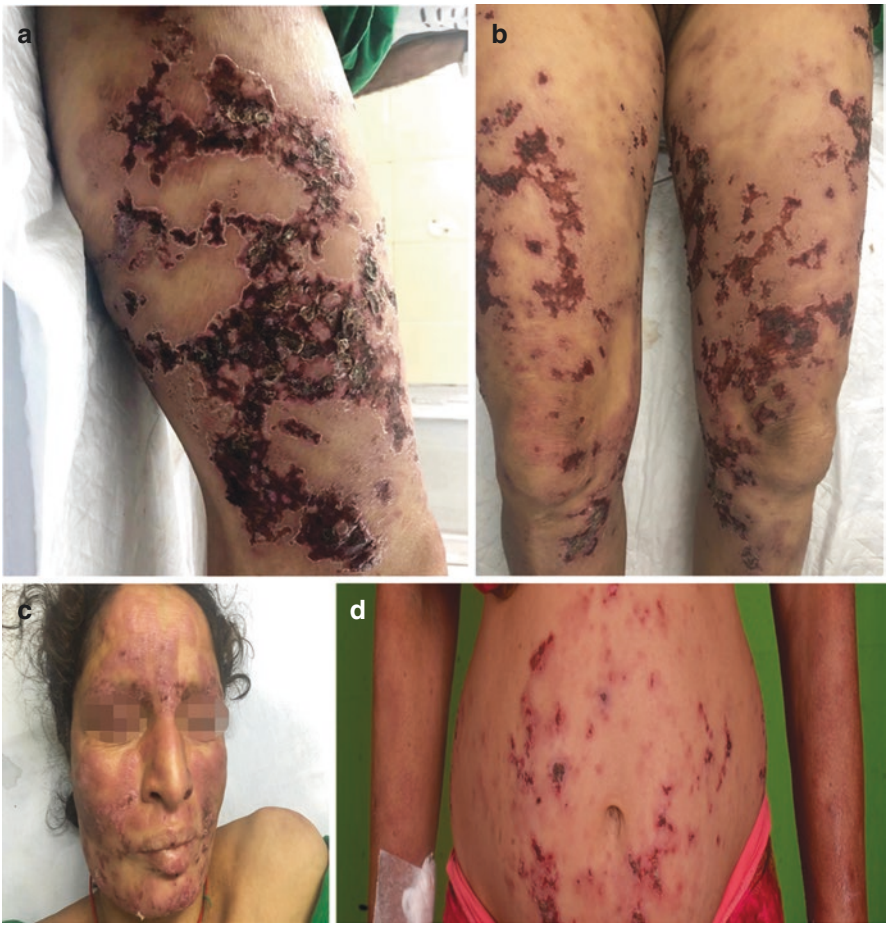

Fig. 31.1 Multiple, coalescing, sharply angulated ulcers with jagged margins and necrotic center overlying erythematous nodulo-plaques on the extremities (**a, b**), face (**c**), and trunk (**d**)

What Is Your Diagnosis?

1. Lucio leprosy with Lucio phenomenon.
2. Purpura fulminans.
3. Antiphospholipid antibody syndrome.
4. Disseminated intravascular coagulation**.**

Investigations

Slit skin smear unveiled a bacteriological index of 4+ and a morphological index of 0%. Hemogram was suggestive of anemia with raised erythrocyte sedimentation rate. Skin biopsies were taken from a nodulo-plaque lesion on the face and the edge of ulcer on the thigh. Histological examination from both revealed dermal edema, collection of foamy histiocytes admixed with neutrophils, and nuclear debris, with perineural inflammation and focal panniculitis, in addition to evidence of leukocytoclastic vasculitis with presence of plump endothelial cells and nuclear debris in the vessel wall (Fig. 31.2a). The biopsy from the edge of the ulcer in addition demonstrated epidermal ulceration and apoptotic keratinocytes. There were numerous acid-fast bacilli, some of which were present within endothelial cells (Fig. 31.2b). Coagulation profile, liver function tests, renal function tests, urinalysis, blood sugar, antinuclear factor, rheumatoid factor, sputum for AFB, Mantoux test, and chest X-ray were normal. Serology for human immunodeficiency virus, syphilis, and hepatitis B surface antigen was negative. Antiphospholipid antibodies came negative. The blood culture didn't show any organisms.

Final Diagnosis

Lucio leprosy with Lucio phenomenon.

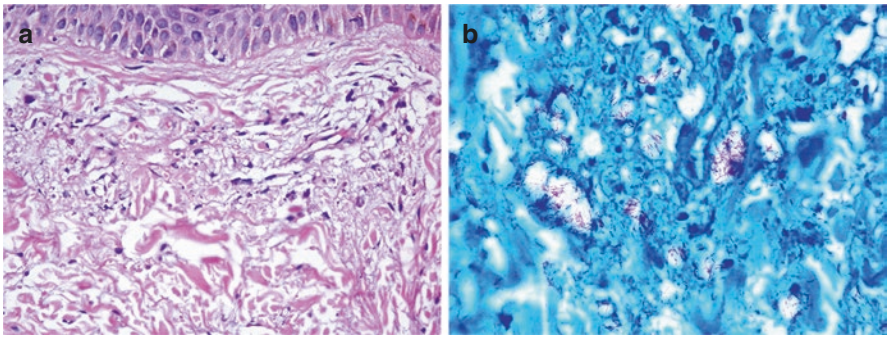

Fig. 31.2 (**a**) Edematous upper dermis with capillaries lined by plump endothelial cells with accompanying foamy cells (Hematoxylin and Eosin, ×200) (**b**) Numerous acid-fast bacilli some of which are within endothelial cells (modified Ziehl-Neelsen stain, ×1000)

Discussion

Lucio leprosy (LuLp) also known as *lepra bonita* ("pretty leprosy" in Spanish) or diffuse leprosy of Lucio and Latapi (first identified by Lucio and Alvarado in 1852 and later described by Latapi and Chevez-Zamora) is a diffuse, non-nodular form of leprosy that is primarily seen in Mexico and Central America with a few cases being reported from Southeast Asian countries and South American, Pacific, Middle East, and African nations [1]. *Mycobacterium lepromatosis*, a species distinct from *Mycobacterium leprae*, has been isolated from patients with diffuse lepromatous leprosy and is believed to be the causative organism for this form of the disease. However, substantial evidence on its role in the pathogenesis of LuLp is still lacking.

The clinical sine qua non is diffuse infiltration of the skin of the face as well as the body without any evidence of discrete or nodular lesions. The prominent skin infiltration leads to obliteration of the skin wrinkles and imparts a shiny and waxy appearance that has been compared to myxedema. Loss of eyebrows, eyelashes, and body hair is frequently observed. As the disease progresses, there may be numbness and edema over the hands and feet. Over time, all of the skin becomes atrophic giving an ichthyosiform appearance to some areas. Infiltration of the mucosa can lead to epistaxis, septal perforation, thickening of the tongue, and hoarseness of voice.

Lucio phenomenon (LP) is a reactional state that is characteristically associated with LuLp; however, it can also occur in the classical nodular form of lepromatous and borderline leprosy. LP is characterized by the presence of purpuric lesions and hemorrhagic bullae that progress to necrotic, multi-angulated, jagged ulcers and eschar formation. The lesions spread in an ascending fashion over the extremities and rarely involve the face and trunk. The ulcers heal over a period of 2–8 weeks leaving behind jagged atrophic scars with a peripheral halo of hyperpigmentation. Systemic symptoms in the form of fever, visceral involvement, or neuritis are characteristically absent and serve as an important clue in differentiating LP from necrotic erythema nodosum leprosum (ENL) which also presents as painful necrotic ulcers [2]. The pathogenesis of LP is believed to be uninhibited multiplication of lepra bacilli in an anergic background and enhanced exposure of mycobacterial antigen to circulating antibodies resulting in diffuse infiltration of the skin and vasculitis, respectively.

The bacteriological and morphological index is high in patients with LP. Two types of patterns have been described in the histopathology of LP: one being leukocytoclastic vasculitis and the other being endothelial cell proliferation and thrombosis. Other common histological findings include ischemic necrosis of the epidermis and dermis and colonization of endothelial cells by acid-fast bacilli. Other laboratory findings that can be observed in LP are anemia, elevated erythrocyte sedimentation rate, hypoalbuminemia, hypergammaglobulinemia, and false-positive serological reaction for syphilis. According to international literature, three defining criteria have been adopted for describing a case of LP: cutaneous ulceration, vascular thrombosis, and invasion of blood vessels by leprosy bacilli.

Table 31.1 Comparison of Lucio phenomenon and erythema nodosum leprosum

	Lucio phenomenon	Erythema nodosum leprosum
Patient profile	Occurs in patients of Lucio leprosy	Occurs in patients with lepromatous leprosy and borderline lepromatous leprosy
Clinical presentation	Irregular, jagged purpuric lesions and ulcers	Nodules and plaques that develop necrosis and painful ulceration
Systemic symptoms, neuritis, and visceral involvement	Uncommon	Frequently present
Histopathology	Ischemic necrosis of the epidermis and dermis, colonization of endothelial cells by acid-fast bacilli, fibrin thrombi in the upper dermal vessels with or without vasculitis	Foamy histiocytes in the dermis, infiltrated by neutrophils, associated with variable vasculitis and panniculitis
Treatment	Multidrug therapy (MB-MDT) Steroids may be required in severe cases Thalidomide ineffective	Corticosteroids in combination with multidrug therapy (MB-MDT) Excellent response to thalidomide

MB-MDT multibacillary multidrug therapy

Differential diagnoses include necrotic ENL, vasculitis, disseminated intravascular coagulation, and deep mycosis. LP can be differentiated from necrotic ENL based on certain clinical and histopathological findings (Table 31.1).

Treatment is based on multidrug therapy (MB-MDT) to which the patients show excellent response. Systemic corticosteroids may be required in severe cases. However, thalidomide and clofazimine are less effective in cases of LP.

References

1. Sharma P, Kumar A, Tuknayat A, Thami GP, Kundu R. Lucio phenomenon: a rare presentation of Hansen's disease. J Clin Aesthet Dermatol. 2019 Dec;12(12):35–8.
2. Chandrashekar L, Kumari R, Thappa D, et al. Is it Lucio phenomenon or necrotic erythema nodosum leprosum? Indian J Dermatol. 2013;58(2):160.

Chapter 32
Asymptomatic Finger Swelling

Maitreyee Panda and Ishan Agrawal

Abstract Leprosy is an ancient disease which is now evolving in terms of its presentation and behaves like a true chameleon. Although the majority of cases are still diagnosed with classical clinical presentations, there are atypical and uncommon presentations of Hansen's which may be misleading and pose diagnostic dilemmas. We report a case presenting with isolated dactylitis, without any classical features of Hansen's, confirmed histopathologically with visualisation of AFB, and a final diagnosis of BT Hansen's, highlighting the presence of atypical manifestations of Hansen's in endemic countries like India.

Keywords BT Hansen's · Dactylitis · Atypical presentation

Clinical Presentation

A 58-year-old female presented with an ill-defined swelling and stiffness of the middle finger of the right hand of 2 months duration. The swelling was insidious in onset and gradually progressive, started near the proximal interphalangeal joint and progressed distally (Fig. 32.1). On examination, patient had movement restriction around the affected joint, with no other joint involvement. There was no pain, tenderness, or local rise in temperature. No other body parts were affected. Patient denied any history of trauma prior to the appearance of swelling. No nerve thickening or hypoaesthesia was noted. Patient denied any drug history prior to the appearance of swelling. She had no known comorbidities including diabetes and hypertension.

M. Panda (✉) · I. Agrawal
Department of Dermatology, IMS and SUM Hospital, Bhubaneswar, Odisha, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_32

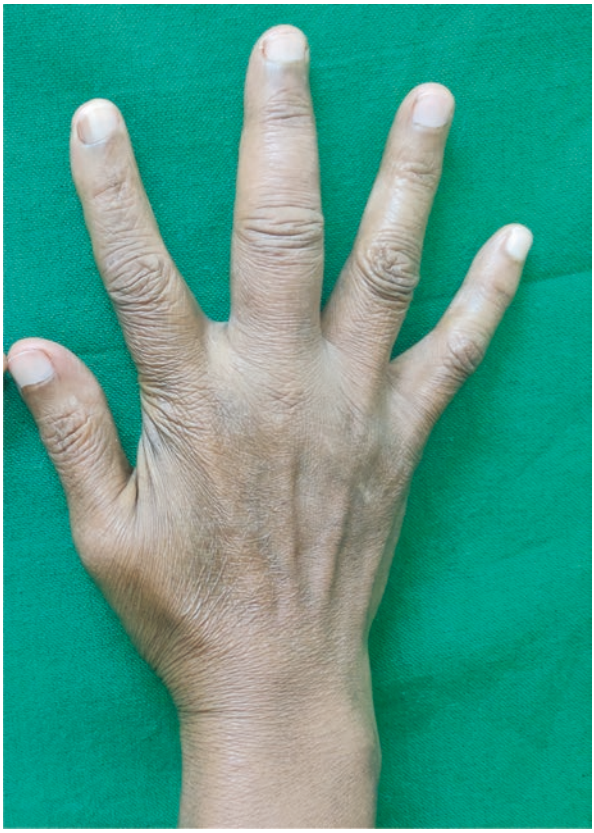

Fig. 32.1 Fusiform swelling present over the proximal half of the right middle finger

What Is Your Diagnosis?

1. Rheumatoid arthritis.
2. Tubercular dactylitis.
3. Lupus erythematosus.
4. Dactylitis in borderline tuberculoid leprosy.

Investigations

X-ray of the right hand revealed mild soft tissue swelling in the middle finger. Chest X-ray revealed no abnormality. Complete blood count, serum uric acid levels, ESR, and CRP were within normal limits. Mantoux test, HIV, hepatitis B serology, ANA, and RF were negative. An FNAC and synovial fluid analysis revealed few inflammatory cells (lymphocytes). KOH mount was negative. With no conclusive reports, a skin biopsy was planned.

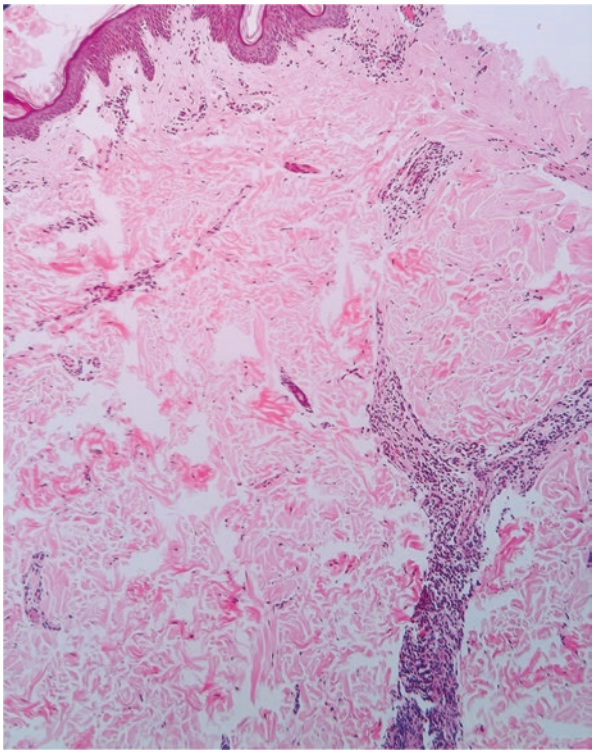

Fig. 32.2 Histopathology showing dermal perivascular and periappendageal chronic inflammatory cell infiltration with lymphocytes, histiocytes, few epithelioid cells, and classical oblong-shaped granulomas (10×, H&E)

A 4 mm skin punch biopsy from the skin over the joint swelling was performed and revealed dermal perivascular and periappendageal chronic inflammatory cell infiltration with lymphocytes, histiocytes, and few epithelioid cells (Fig. 32.2). Wade fine stain revealed acid-fast bacilli with bacterial index of 1+. Slit skin smear did not reveal any bacilli.

Final Diagnosis

Borderline tuberculoid Hansen's disease with monoarticular swelling and not in reaction.

Discussion

Early diagnosis and treatment in leprosy are important for disease control and prevention of physical disabilities, which heavily impacts the occupational, social, and personal life of an individual [1]. Leprosy is known to mimic various

rheumatological disorders; however, these are underreported manifestations of an otherwise common disease. Clinical presentation of leprosy may simulate diseases like rheumatoid arthritis, reactive arthritis, psoriatic arthritis, and gout [2].

Arthritis and arthralgia are known constituents of the frequently seen lepra reactions, where the underlying pathogenesis is often inflammatory arthritis [3]. However, numerous other hypotheses may explain the insidious development of subcutaneous swelling as a part of the primary disease. Slow-growing bacteria such as mycobacteria can induce and sustain arthritis.

Infection causing activation of T lymphocytes leads to production of lymphokines that trigger B lymphocytes to produce agalactosyl immunoglobulins causing chronic inflammation in synovial tissues [4].

Other mechanisms include direct tissue infiltration by microbes and induction of autoimmune phenomenon by mycobacteria with cross-reactivity between 65kD mycobacterial protein and cartilage proteoglycans, as suggested previously [5]. This arthritis has been observed in patients with resolved leprosy and paucibacillary leprosy, in non-reaction states. Owing to these disease processes, occasionally rheumatological manifestations maybe the initial presenting feature of leprosy [5].

Mycobacterial infections can simulate a similar clinical picture with subcutaneous swellings in localised areas due to exogenous localised infection. Exclusion of cutaneous tuberculosis and atypical mycobacterial infection is done with the absence of acid-fast bacilli on ZN staining of the tissue biopsy specimen [6].

Dactylitis and tenosynovitis have been reported in other mycobacteria also including *Mycobacterium tuberculosis* and *Mycobacterium haemophilum* [7, 8].

Other infective differentials include deep fungal infections like pheohyphomycosis and sporotrichosis, which may clinically present as subcutaneous nodules or swellings over exposed parts of the body such as the extremities. The diagnosis of deep tissue fungal infections is confirmed with histopathological presence of multiple granulomas and visible fungal elements on staining with fungal stains (like Gomori methenamine stain) [9].

Lesser seen bacterial infectious granulomatous diseases may present similarly. These include botryomycosis presenting as subcutaneous nodules that progress into fluctuant masses and sinuses. Other close differentials include actinomycosis and eumycetoma. The diagnosis in these conditions is confirmed by Gram staining, growth of causative organism on culture, and presence of granulomas on tissue histopathology [10].

The backbone of diagnosis of BT Hansen's rests on the fundamental findings of hypopigmented patch, hypoaesthesia, and nerve thickening. However, our case highlights a distinctly atypical manifestation of leprosy where the patient has presented with isolated finger swelling without any visible cutaneous manifestations or any nerve thickening. Standard treatment multidrug therapy (MDT) with rifampicin, clofazimine, and dapsone was for 12 months. The patient showed significant improvement after 3 months of MDT (Fig. 32.3).

In endemic regions, there must be a high degree of suspicion, and Hansen's must be kept as a clinical differential, however remote. Moreover, early disease identification and timely therapeutic intervention can prevent disease spread, morbidity, and disabilities.

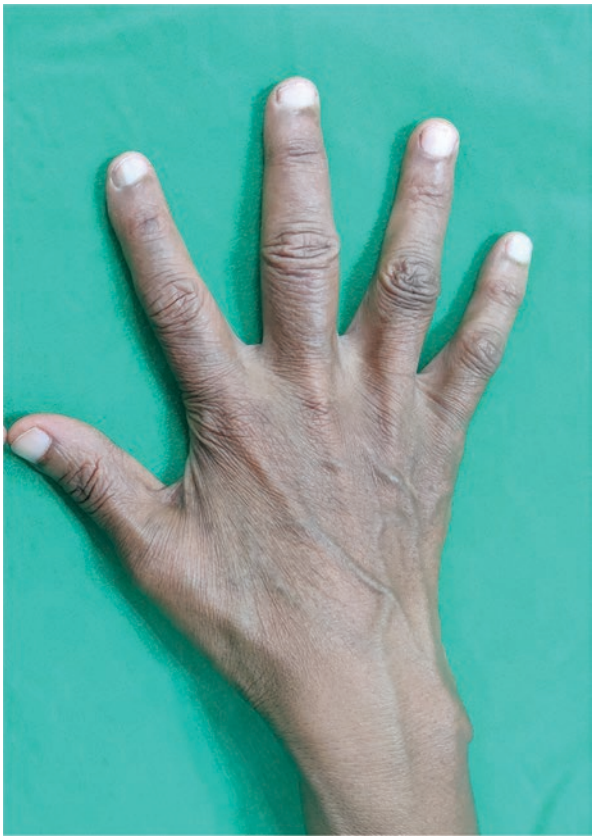

Fig. 32.3 Visible wrinkling over the right middle finger, indicating decrease in the swelling, after 12 weeks of MDT initiation

References

1. Jerajani HR. IAL textbook of leprosy–Hemanta Kumar Kar and Bhushan Kumar. Indian J Dermatol Venereol Leprol. 2010;76:309–10.
2. Gupta S, Li C, Thallapally V, et al. Chronic hand swelling and dactylitis in leprosy: a case report and review of the literature. Cureus. 2021;13:e13451.
3. Sarkar RN, Phaujdar S, Banerjee S, Siddhanta S, Bhattacharyya K, De D, et al. Musculoskeletal involvement in leprosy. Indian J Rheumatol. 2011;6:20–4.
4. Wakhlu A, Sawlani KK, Himanshu D. Rheumatological manifestations of Hansen's disease. Indian J Rheumatol. 2018;13:14–9.
5. Cossermelli-Messina W, Cossermelli W. Possible mechanisms of chronic leprosy-related arthritis. Sao Paulo Med J. 1997;115:1406–9.
6. Frankel A, Penrose C, Emer J. Cutaneous tuberculosis: a practical case report and review for the dermatologist. J Clin Aesthet Dermatol. 2009;2:19–27.
7. Thatoi P, Parida M, Barik R, Das B. Multifocal tubercular dactylitis: a rare presentation of skeletal tuberculosis in an adult. J Clin Diagn Res. 2017;11:OD23–4.

8. Woodworth MH, Marquez C, Chambers H, Luetkemeyer A. Disabling Dactylitis and tenosynovitis due to mycobacterium haemophilum in a patient with human immunodeficiency virus/acquired immune deficiency syndrome. Open Forum Infect Dis. 2017;4:165.
9. Chintagunta S, Arakkal G, Damarla SV, Vodapalli AK. Subcutaneous phaeohyphomycosis in an immunocompetent individual: a case report. Indian Dermatol Online J. 2017;8:29–31.
10. Devi B, Behera B, Dash ML, Puhan MR, Pattnaik SS, Patro S. Botryomycosis. Indian J Dermatol. 2013;58:406.

Chapter 33
Generalized Erythematous Edematous Plaques and Nodules

Anup Tiwary

Abstract There are many atypical presentations of leprosy and lepra reactions which need meticulous examination and high index of suspicion to avoid the misdiagnosis and delay in management. One such rare case of type 2 lepra reaction in a pregnant woman is presented here who had no history of any anti-leprosy medications or leprosy.

Keywords Erythema nodosum leprosum · T2LR · Pregnancy · Atypical

Clinical Presentation

A 29-year-old married female presented with fever, arthralgia, and generalized rash for about 1 month. She had three children and was 8 months pregnant at the time of presentation in the skin outpatient department. She was apparently well 1 month before when erythematous lesions started developing on both lower limbs which progressively involved the upper limbs, trunk, and face. Mild fever, joint pain, and generalized body ache were the associated complaints. Cutaneous examination revealed erythematous and violaceous and variably sized, non-scaly, nodules and plaques on both upper and lower limbs, chest, abdomen, back, and face (including ears) (Fig. 33.1a–d). Palmoplantar skin, axilla, groin, genitalia, and mucosa were spared. All the lesions were firm and mildly tender on palpation. On peripheral nerve examination, both ulnar nerves were thickened (grade 1) and tender (grade 1), but no sensorimotor deficits were found. Pallor, bilateral pitting edema on the hands and feet, and bilateral inguinal lymphadenopathy were also noted on general physical examination. Systemic examination was normal. There was no personal or family history of similar skin lesions. History of any chronic illness or drug intake was also absent.

A. Tiwary (✉)
Yashoda Hospital and Research Center, Ghaziabad, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_33

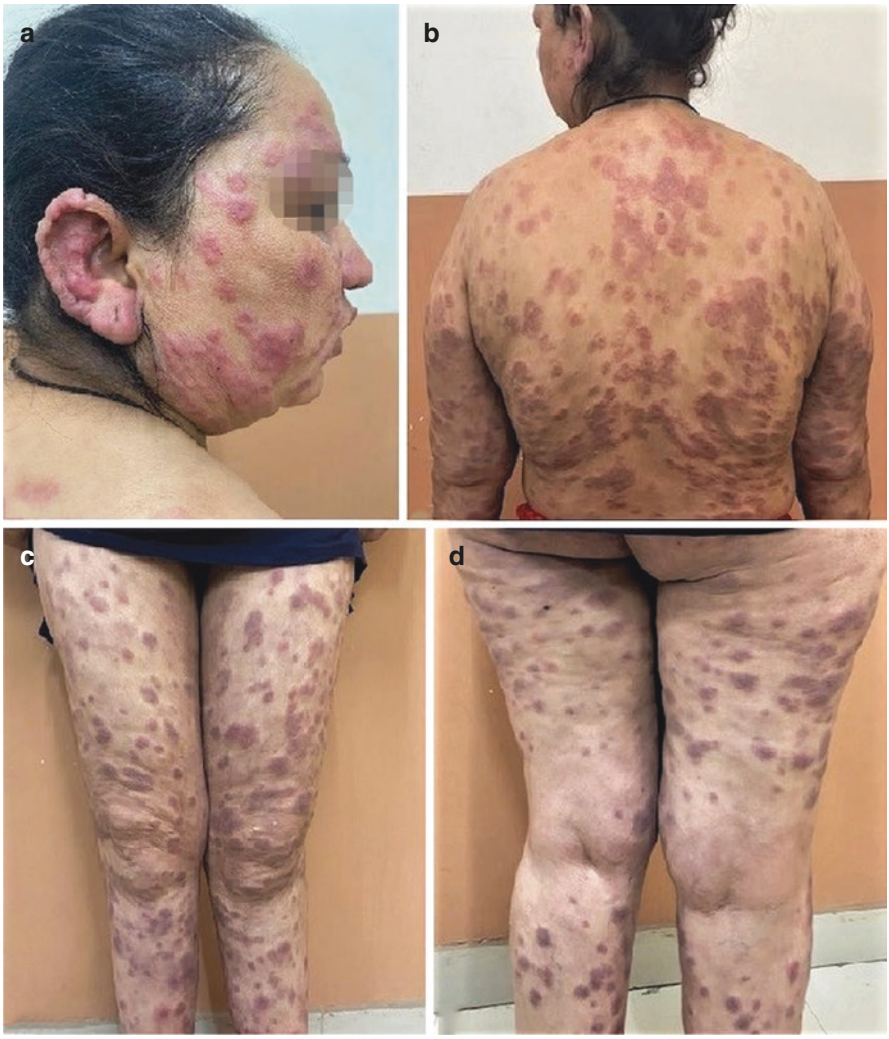

Fig. 33.1 (**a–d**) Generalized, bilateral, erythematous nodules and plaques

What Is Your Diagnosis?

1. Erythema nodosum leprosum.
2. Sweet's syndrome.
3. Sarcoidosis.

Investigations

All routine hematological and urinary investigations were done which showed mild anemia (Hb 11.1 gm/dl), neutrophilia (87%), hypoalbuminemia, mild albuminuria, and elevated liver enzymes (serum aspartate aminotransferase, 139 U/L, and alanine aminotransferase, 207 U/L; alkaline phosphatase, 390 U/L, and gamma-glutamyl transferase, 212 U/L). Slit skin smears (from ear lobe and a plaque on forearm) showed 2+ bacilli. Histopathology demonstrated nodular granulomatous inflammation centered around neurovascular bundles of superficial and deep dermis (Fig. 33.2). The granuloma consisted of foamy macrophages and lymphocytes. Also, neutrophils dotted the granulomas accompanied by scant nuclear dust and fibrin. The dermoepidermal junction was spared by the granulomatous infiltrate.

Final Diagnosis

Lepromatous leprosy with erythema nodosum leprosum (ENL).

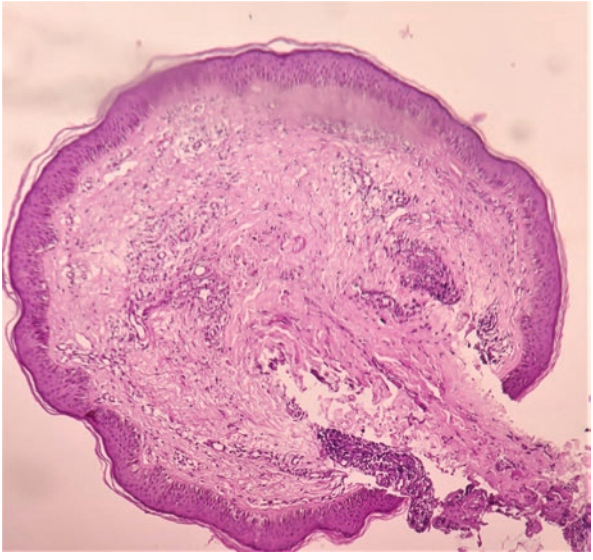

Fig. 33.2 Nodular granulomatous inflammation in superficial and deep dermis consisting of foamy macrophages, lymphocytes, and neutrophils (H&E × 200)

Discussion

Hansen's disease or leprosy is a great imitator which has protean clinical manifestations. Based upon the cutaneous and nerve involvement followed by microscopy of slit skin smear, it is broadly classified into paucibacillary, multibacillary, and reactionary states. The pathogenesis is much more complex than it was understood decades before. The immune status and genetic makeup of the patients are the key determinants for the acquisition of infection, clinical spectrum, course of the disease, and response to treatment [1].

Type 1 lepra reactions (T1LR) and type 2 lepra reactions (T2LR) or ENL are well-known exaggerated immune responses seen in borderline and lepromatous spectrum, respectively. These reactions usually occur after initiating anti-leprosy treatment (ALT), but their pathogenesis differs [1]. The age-old theory behind T2LR mainly revolves around antigen (released after starting treatment)-antibody complex formation [2]. It was an oversimplified concept which could not explain many things in some cases of T2LR such as the absence of treatment history, poor response to many immunosuppressives, recurrence for many years even after completing multidrug therapy (MDT), and correlation of many different serum biomarkers with severity of T2LR which suggested the indispensable role of T cells, neutrophils, and innate immunity too. The ALT-induced release of fragmented *Mycobacterium leprae* antigens potentially upregulate the expression of CD64 surface receptors on neutrophils leading to secretion of many cytokines, immune complex formation, and eventually tissue damage [2]. However, certain triggering factors do exist such as systemic infections or illness, stress, and vaccination which can directly stimulate neutrophils to ultimately culminating in T2LR. Of note, pregnancy is another such triggering condition which increases the risk of T2LR, probably due to systemic immunosuppression leading to high bacillary load [3]. Atypical clinical course of leprosy and ENL in pregnancy are usually attributed to the altered secretion of steroids and hormonal and metabolic changes [3].

Herein, the patient was pregnant and presented with T2LR with no history of ALT or leprosy itself which has been rarely reported in previous literature. Moreover, generalized distribution of typical ENL lesions involving the face, whole trunk, and both upper and lower limbs is also uncommon which was observed in this patient. Such clinical deviations from classical presentations indicate the complex interplay of genetics, cell-mediated immunity, humoral immunity, and mycobacterium leprae [1].

A high index of suspicion is always warranted in any atypical case of T2LR to avoid the delay in diagnosis and treatment. Standard MDT is safe to start in pregnancy with ENL, and the benefit of systemic steroids in the third trimester usually outweighs the risk if left untreated. Within 4 weeks of starting standard three-drug MDT and oral prednisolone (30 mg/day for 2 weeks and then 20 mg/day for 2 weeks), a significant improvement was seen in this patient (Fig. 33.3a, b). A multidisciplinary approach involving obstetrician and neonatologist should always be preferred to avoid any complication in mother or fetus [4].

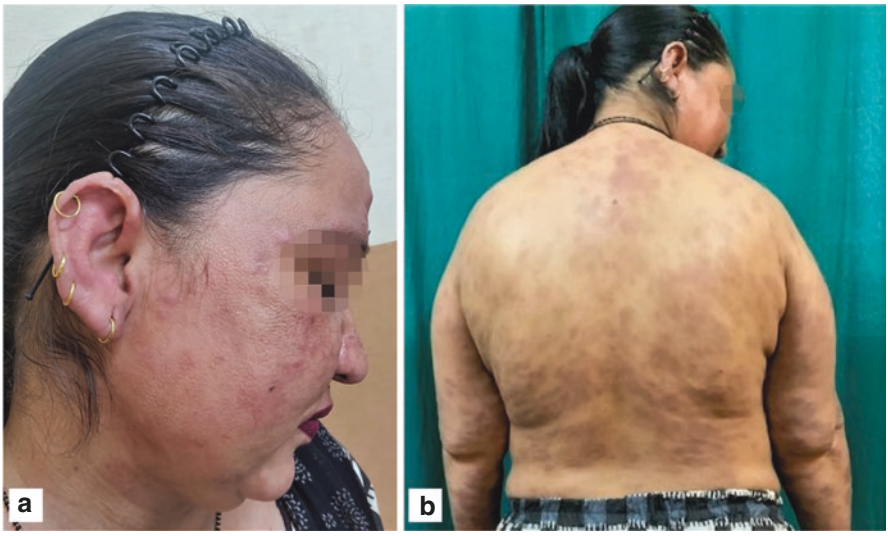

Fig. 33.3 (**a, b**) Clinical improvement after MDT and steroids

References

1. Pandhi D, Chhabra N. New insights in the pathogenesis of type 1 and type 2 lepra reaction. Indian J Dermatol Venereol Leprol. 2013;79:739–49.
2. Bhat RM, Vaidya TP. What is new in the pathogenesis and management of erythema nodosum leprosum. Indian Dermatol Online J. 2020;11:482–92.
3. Vijay N, Sarma S. Leprosy with erythema Nodosum Leprosum in pregnancy: a rare phenomenon! J South Asian Feder Obst Gynae. 2019;11(5):329–30.
4. Ozturk Z, Tatliparmak A. Leprosy treatment during pregnancy and breastfeeding: a case report and brief review of literature. Dermatol Ther. 2017;30(1):e12414-1–2.

Chapter 34
Generalized Pustulo-Ulcerative Lesions

Abhishek Parekh, Jatin Chauhan, and Hiral Shah

Abstract Uncommon variants of lepra reactions can be very commonly misdiagnosed in patients especially in those who have not been previously diagnosed with leprosy. A high index of suspicion is always warranted in any atypical case of lepra reaction to avoid the delay in diagnosis and resulting morbidity. Here, we present one such rare case of type 2 lepra reaction in a 39-year-old female.

Keywords Erythema nodosum leprosum · Type 2 lepra reaction · Pustular · Atypical

Clinical Presentation

A 39-year-old female presented with fever, arthralgia, and skin lesions throughout her whole body for 8 days. She was apparently alright 8 days back, after that multiple, tiny, reddish, elevated, painful lesions started developing on her forearms which progressively involved both arms, lower limbs, chest, abdomen, back, and buttocks. After 4–5 days, the lesions turned into pustules. These lesions were associated with fever and arthralgia, relieved on medication.

The patient gave history of similar episode 18 months back for which she took some undocumented medication. She was diagnosed as a case of lepromatous leprosy 1 month back and was prescribed WHO MDT MB pack which she took irregularly. Family history of leprosy was there in one of her second-degree relatives.

Cutaneous examination revealed multiple, erythematous, variable sized, tender, papules, plaques, and nodules surmounted with pustules present over the chest, abdomen, back, buttocks, and both upper limbs and lower limbs (Fig. 34.1a–c). Palmoplantar skin, axilla, groin, genitalia, and mucosa were spared. Bilateral ulnar, superficial radial, common peroneal, and tibial nerves were thickened, but

A. Parekh · J. Chauhan · H. Shah (✉)
Department of Dermatology, Venereology and Leprosy, S.S.G. Hospital, Vadodara, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_34

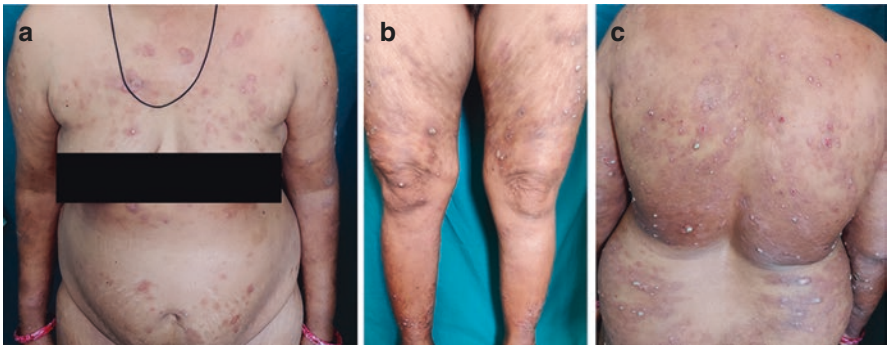

Fig. 34.1 (**a–c**) Multiple, erythematous, variable-sized papules, plaques, and nodules surmounted with pustules present over the chest, abdomen, back, and both lower limbs

non-tender. There was no significant lymphadenopathy. Systemic examination was unremarkable except for bilateral pedal edema.

What Is Your Diagnosis?

(a) Pustular erythema nodosum leprosum in lepromatous leprosy.
(b) Sweet syndrome.
(c) Acute generalized exanthematous pustulosis (AGEP).
(d) Pustular psoriasis.

Investigations

- The hematological examination revealed mild anemia (Hb 9.9 gm/dl), leukocytosis (22,400/cu.mm) with neutrophilia (88%), thrombocytosis (7,27,000/cu.mm), raised ESR (40 mm after first hour), and CRP (192 μg/ml). Hypoalbuminemia and mild albuminuria were also noted.
- Her blood and pus cultures were sterile.
- Ziehl-Neelsen (ZN) stain of slit skin smear (SSS) from lesional skin and right ear lobe was negative; however, ZN stain of smear made from pustular lesion showed plenty of granular bacilli with neutrophils (bacillary index, BI, 4+) (Fig. 34.2).
- Biopsy taken from erythematous plaque showed atrophic epidermis, upper dermal edema, perivascular and periadnexal macrophage granulomas, and neutrophilic infiltration with vasculitis (Fig. 34.3a, b). Fite-Faraco (FF) stain did not

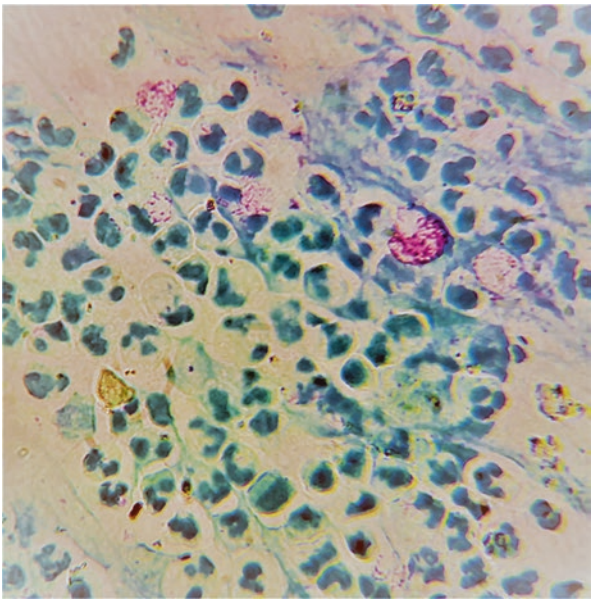

Fig. 34.2 ZN stain of smear made from pustular lesion showed plenty of granular bacilli with neutrophils (bacillary index, BI, 4+)

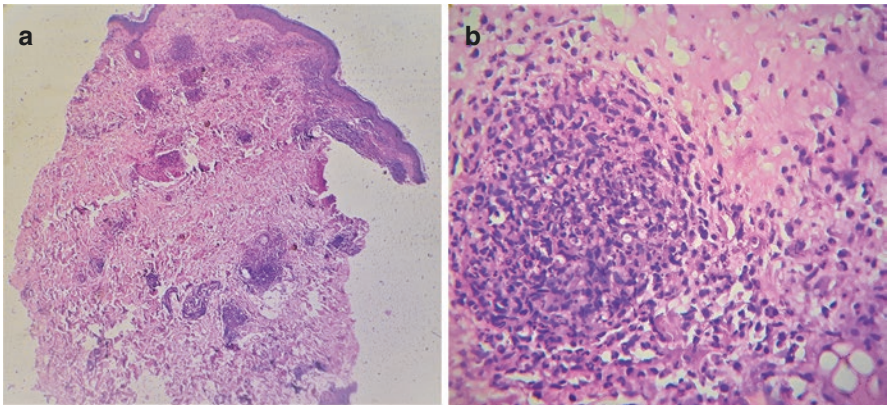

Fig. 34.3 (**a**) (4x) (**b**) (40×) H&E: Histopathology of erythematous plaque demonstrated atrophic epidermis, upper dermal edema, perivascular and periadnexal macrophage granulomas, neutrophilic infiltration with vasculitis

show any acid-fast bacilli. The biopsy from the pustular lesion revealed atrophic epidermis, dermal edema with neutrophilic infiltration, perivascular and periadnexal curvilinear macrophage granuloma, and globi seen as bluish-gray material in foamy macrophages (Fig. 34.4a, b). FF stain of the pustular lesion showed solid and fragmented bacilli in macrophage granuloma (Fig. 34.5).

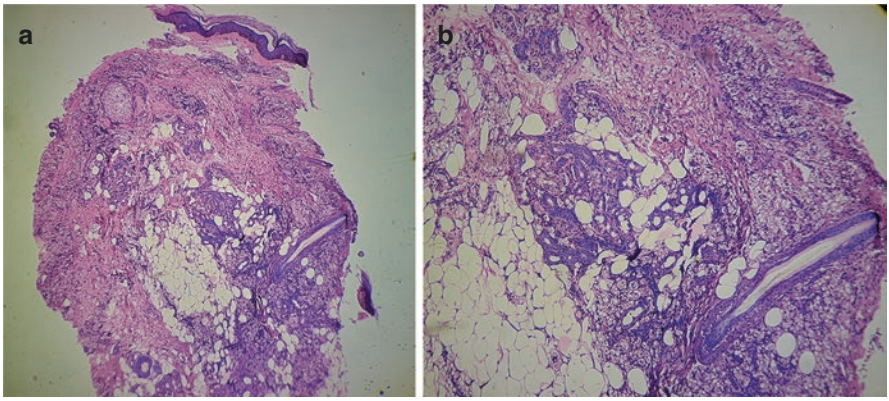

Fig. 34.4 (**a**) (4×), (**b**) (10×) H&E: Histopathology of pustular lesion demonstrated atrophic epidermis, dermal edema with neutrophilic infiltration, perivascular and periadnexal curvilinear macrophage granuloma, globi seen as bluish-gray material in foamy macrophages. (Inset in 4a: sub-epidermal collection of neutrophils)

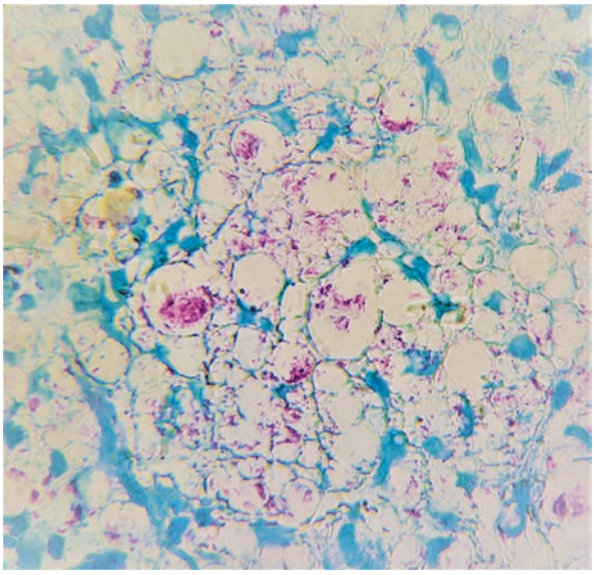

Fig. 34.5 FF stain of pustular lesion showed solid and fragmented bacilli in macrophage granuloma

Final Diagnosis

Pustular erythema nodosum leprosum (ENL) in lepromatous leprosy.

Discussion

Erythema nodosum leprosum (ENL) is a type III hypersensitivity reaction, which causes inflammation of the skin, nerves, and other organs [1]. It typically occurs at the sites of small, often clinically inapparent, regressing lepromatous granulomas [2]. It is hypothesized that a high release of bacterial antigen load leads to formation of immune complexes, which are deposited in vessel walls, nerves, and other organs, resulting in protean manifestation of ENL [3]. It is mediated through CD4+ Th2 cells, and cytokines involved here are IL4, IL5, IL13, TNF-alpha, and IFN-gamma. Cell-mediated immunity also plays a role in pathogenesis of ENL [1]. The usual triggers associated with ENL reaction include surgical interventions, pregnancy, parturition, lactation, menstruation, trauma, intercurrent illness, vaccination, and physical or mental stress [1]. It is more commonly seen in patients of lepromatous leprosy with skin infiltration, those who are on anti-leprosy drugs except clofazimine, patients <40 years of age, and bacillary index (BI) >4+ [1].

Recurrent crops of tender, evanescent, erythematous to coppery papules, plaques, or nodules associated with fever and other constitutional symptoms characterize classic ENL, which usually lasts for 7–10 days [3]. Extracutaneous manifestations include fever with constitutional symptoms, neuritis, tender lymphadenopathy, arthritis, epididymo-orchitis, dactylitis, synovitis, iridocyclitis, rhinitis, epistaxis, and, rarely, laryngeal edema, glomerulonephritis, acute adrenal insufficiency, and hemolytic crisis [3].

Less commonly, the lesions may be hemorrhagic, vesiculobullous, erythema multiforme-like, pustular, or ulcerated [3]. Uncommon variants of ENL can be very commonly misdiagnosed in patients, especially in those who have not been previously diagnosed with leprosy [2].

Pustular variant of ENL is the manifestation of very high bacillary load. Here, pus consists of a cheesy material, which on acid-fast staining reveals granular acid-fast bacilli (AFB) and plenty of polymorphonuclear cells, some of which may contain bacilli [4]. The pus is sterile on culture for pyogenic organisms but contains AFB in various stages of degeneration. This finding suggests an immunological genesis of pustulation, and not by a pyogenic secondary organism [4]. These lesions may be contagious enough to transmit Hansen's disease [2]. Some have even described the phenomenon of elimination of bacilli from inside out [2]. Pustular lesions ulcerate most of the time and may lead to erythema necroticans leprosum.

Herein, the patient was presented with pustular lesions over the trunk and extremities. After 4 to 5 days, some of these lesions became ulcerated. After confirming the diagnosis, she was put on RO therapy (rifampicin + ofloxacin) for 28 days as BI was 4+ [5]. Adult multibacillary blister pack was continued. She was given thalidomide (100 mg) three times a day. Injectable dexamethasone 8 mg was given along with supportive treatment for 1 week. Dexamethasone was tapered to 6 mg as response to thalidomide became obvious and continued for another 1 week. After 2 weeks of therapy, pustular lesions subsided (Fig. 34.6a–c). Patient was discharged with 30 mg prednisolone and thalidomide (100 mg) twice a day.

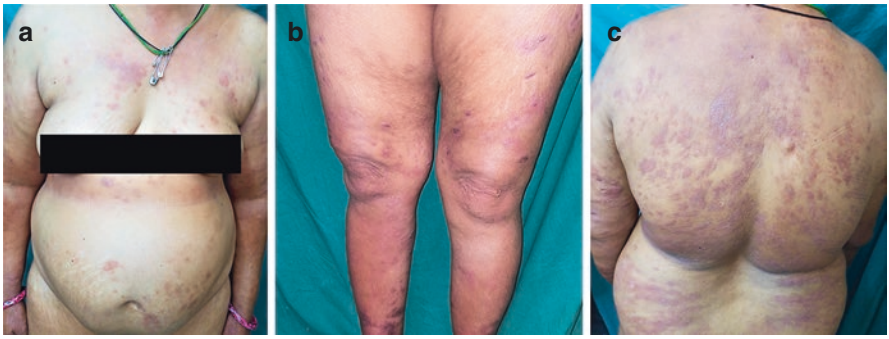

Fig. 34.6 (**a–c**) Clinical improvement after 2 weeks of therapy

A high index of suspicion is always warranted in any atypical case of T2LR to avoid the delay in diagnosis and resulting morbidity.

References

1. Kumar H, Chauhan A. Leprosy reactions: pathogenesis and clinical features. In: Kumar B, Kumar H, editors. IAL textbook of leprosy. 2nd ed. New Delhi: Jaypee Brothers Medical Publishers; 2017. p. 412–135.
2. Ridley D, Job C. The pathology of leprosy. In: Hastings R, editor. Leprosy. New York: Churchill Livingstone publishing; 1985. p. 100–30.
3. Dave S, Thappa D, Nori A, Jayanthi S. A rare variant of erythema nodosum leprosum: a case report. Dermatol Online J. 2003;9(5):11.
4. Ramu G. Acute exacerbations (reactions) in leprosy. In: Dharmendra, editor. Leprosy in India. Mumbai: Kothari Medical publishing; 1978. p. 108–37.
5. Katoch K. New emerging drug regimens for leprosy. Indian J Dermatol Venereol Leprol. 1997;63:130–47.

Chapter 35
Acral Nodules in an Elderly Male

Niharika Ranjan Lal and Piyush Kumar

Abstract An elderly male presented with asymptomatic nodules on the hands and feet of 1 year duration. A few similar lesions were noted on the chest too. There was symmetrical and bilateral loss of sensation over the hands and feet, up to mid-forearm and mid-calf level. However, there were no facial lesions, ear lobe infiltration, or madarosis. Histoid leprosy and lepromatous leprosy were considered as clinical differentials, and biopsy from the nodule on the hand was done. Biopsy showed dense nodular monomorphous infiltrate of foamy histiocytes involving the reticular dermis and sparing the upper dermis. Slit skin smear from the lesion showed acid-fast bacilli in clumps with BI >5+. On clinicopathological correlation, diagnosis of lepromatous leprosy was made.

Keywords Leprosy · Lepromatous leprosy · Histoid leprosy · Acid-fast bacilli · Acral nodules

Clinical Presentation

A 50-year-old male from an endemic area presented raised skin lesions over the hands and feet for 1 year. Lesions first appeared on the dorsum of both hands followed by feet and progressed to attain the present status. There was no history of fever with painful red eruptions, joint pain, muscle pain, or nasal stuffiness. He had no difficulty in holding or lifting small objects, and there was no complaint of slipping of footwear while walking. He gave no history of spontaneous blistering or ulcerations. He had not suffered from kala azar in the past and was non-diabetic. There was no family history of similar lesions.

N. R. Lal
ESI-PGIMSR and ESIC Medical College, Kolkata, India

P. Kumar (✉)
Dermatology Venereology and Leprosy, Madhubani Medical College and Hospital, Bihar, India

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7_35

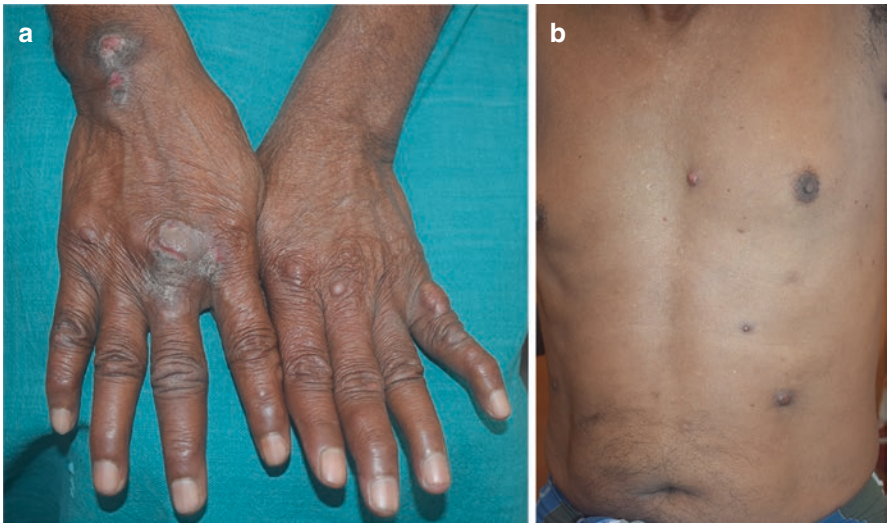

Fig. 35.1 (**a**) Bilateral firm skin-colored nodules on the dorsum of the hands. The right hand additionally shows two pigmented nodules of prurigo nodularis (**b**) Few skin-colored nodules on the trunk

Cutaneous examination revealed multiple skin-colored, non-tender, smooth surfaced, firm papules and nodules symmetrically distributed over the dorsum of both hands and feet and few similar lesions on the chest. Nodules over the dorsum of the hands were more distributed over the interphalangeal and carpometacarpal joints (Fig. 35.1a, b). Ear lobes were spared, and there was no madarosis. No callosity, blisters, or ulcers were observed on either palms or soles. Nerve examination revealed symmetric thickening of common peroneal, ulnar, and radial nerves of all four limbs. There was symmetrical and bilateral loss of sensation over the hands and feet, up to mid-forearm and mid-calf level. Claw-like deformity of the distal interphalangeal joint of the little finger right hand was seen which was attributed to a trauma suffered few years back. Froment's sign was positive more on the left than side (elicited by positive card test). The power of muscles of the feet was within normal range. The gait was normal.

What Is Your Diagnosis?

- Lepromatous leprosy.
- Erythema elevatum diutinum.
- Rheumatoid nodules.
- Multicentric reticulohistiocytosis.

Investigations

Routine hematological and biochemical investigations including urine, renal, and liver function were within normal range. Slit skin smear from the lesion showed acid-fast bacilli and globi with a bacterial index of >5+. Lesional biopsy revealed nodular dense monomorphous granulomatous infiltrate of foamy histiocytes with uniform and sparse scattering of lymphocytes involving the reticular dermis sparing the appendages and upper epidermis. The sub-epidermal papillary dermis (grenz zone) was spared by the infiltrate. Several histiocytes containing bluish staining foamy material and a few foamy giant cells were also seen in the infiltrate (Fig. 35.2a, b). In the deep dermis, the granuloma followed the neurovascular bundle.

Final Diagnosis

Lepromatous leprosy.

Discussion

The clinical differentials of acral subcutaneous nodules include gout, rheumatoid nodules, multicentric reticulohistiocytosis, erythema elevatum diutinum, and calcinosis cutis among others. In endemic areas, lepromatous leprosy (LL), histoid leprosy, and nodular post-kala-azar dermal leishmaniasis need to be included in the list of clinical differentials [1].

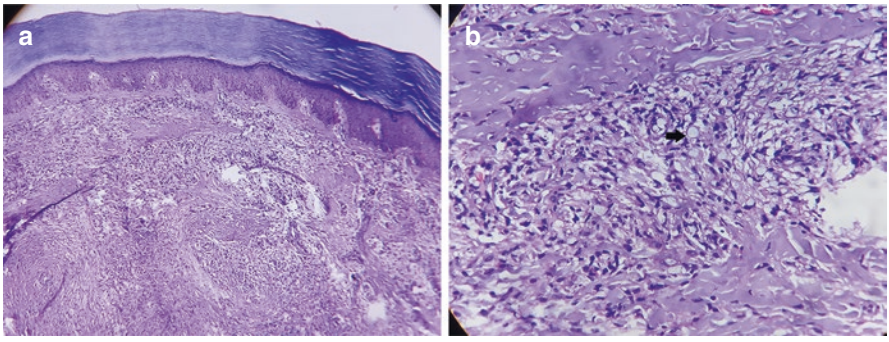

Fig. 35.2 (**a**) Grenz zone and diffuse infiltration of the dermis with foamy histiocytes (H&E × 100) (**b**) Sheets of foamy histiocytes in the dermis. Though demonstration of AFB requires special stains, clumps of AFB on hematoxylin and eosin (H&E) stain may be visualized as blue-gray intracellular structures (arrow) (H&E × 400)

In lepromatous leprosy (LL), *M. leprae* multiplies and spreads extensively because of the absence of cellular immune response to the bacillus. Skin lesions tend to be multiple and symmetrical, preferably located in the colder areas of the body, characterized by hypochromic, erythematous, or bright brownish spots with indefinite borders. These spots may not show loss of sensation. Multiple peripheral nerves are involved in a symmetrical manner. As the disease progresses, lesions infiltrate deeper forming plaques and nodules. In the advanced stages of the disease, the patient's face has a peculiar appearance (leonine facies). Mucous membranes, eyes, bones, joints, lymph nodes, blood vessels, upper airways, teeth, and internal organs may be affected. Though LL is characterized by widespread lesions, sometimes localized lesions including solitary or a few lesions may be the presentation of LL [2, 3].

Histoid leprosy occurs in lepromatous patients who relapse after the dapsone monotherapy in presence of dapsone resistance or rarely de novo. Responsible factors may include resistance to dapsone, irregular and inadequate therapies, or mutant organism *histoid bacillus*. Clinically, it is characterized by cutaneous or subcutaneous nodules and papules, which are painless, firm, discrete, smooth, globular, and skin-colored to yellowish-brown, with apparently normal skin surrounding it. Clinically histoid leprosy may resemble lepromatous leprosy, but the former is distinguished by unique histopathological findings: a leproma consisting of fusiform histiocytes arranged in a tangled or storiform pattern containing acid-fast bacilli. AFB are uniform solid stained and longer than normal bacilli with the absence of globi [4].

The diagnosis of lepromatous leprosy in the absence of characteristic findings like widespread lesions, madarosis, ear lobe infiltration, etc. becomes challenging. One needs to have a high index of suspicion, and biopsy along with slit skin smear can help in arriving at a diagnosis. In our case, the patient was treated with WHO multidrug therapy multibacillary regimen for 12 months.

References

1. Tandon S, Sardana K, Malhotra P, Singh J. Multiple asymptomatic juxta-articular nodules mimicking tuberous-xanthoma-a unusual presentation of Tophaceous gout. J Cutan Aesthet Surg. 2017;10(4):223–5.
2. Lastória JC, Abreu MA. Leprosy: review of the epidemiological, clinical, and etiopathogenic aspects–part 1. An Bras Dermatol. 2014;89(2):205–18.
3. Shenoy SM, Shenoy MM. Mid-borderline leprosy. Indian Dermatol Online J. 2013;4(2):162. https://doi.org/10.4103/2229-5178.110647.
4. Pandey P, Suresh MS, Vk D. De novo histoid leprosy. Indian J Dermatol. 2015;60(5):525.

Index

S. Pradhan, P. Kumar (eds.), *Clinical Cases in Leprosy*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08220-7