Indonesian Dental Association

Journal of Indonesian Dental Association

http://jurnal.pdgi.or.id/index.php/jida
ISSN: 2621-6183 (Print); ISSN: 2621-6175 (Online)

Case Report

The Forgotten Infection Cases: Leprosy Disease Oral Manifestations and Its Problem

Nurfianti[1§], Harum Sasanti[2], Endah Ayu Tri Wulandari[3], Ahmad Ronal[1], Anandina Irmagita[2], Faezah Rokhani[4]

[1] *Department of Oral Medicine, Faculty of Dentistry, Universitas YARSI, Jakarta, Indonesia*
[2] *Department of Oral Medicine, Faculty of Dentistry, Universitas Indonesia, Depok, Indonesia*
[3] *Department of Dentistry, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia*
[4] *Department of Oral Medicine, Faculty of Dentistry, Universiti Sains Islam Malaysia, Malaysia*

KEYWORDS

Early detection, gingivitis, leprosy, *Mycobacterium leprae*, oral manifestation

ABSTRACT

Introduction: Leprosy, an infectious disease caused by Mycobacterium leprae, predominantly affects the skin, peripheral nerves, and mucous membranes. Although highly contagious, most people are naturally resistant. Indonesia ranks third globally in leprosy cases, and the disease continues to pose a significant public health challenge. **Objective:** This report aims to highlight the oral manifestations of leprosy to aid in early detection and treatment, which are essential to prevent disability and stigma. **Case(s):** Five patients diagnosed with borderline lepromatous or lepromatous leprosy were examined, presenting with oral manifestations such as gingivitis, periodontitis, ulceration, epithelial desquamation, anesthesia, and hypopigmented lesions. Poor oral hygiene, observed in several cases, worsened these symptoms. Each patient received multidrug therapy with rifampicin, dapsone, and clofazimine, along with systemic medications as needed. Dentists focused on improving oral hygiene, patient education, and treatments like antiseptic rinses and localized care for ulcers and gingival inflammation to support healing and prevent complications. **Discussion:** The oral manifestations observed in these cases, such as ulceration and epithelial desquamation, are characteristic of advanced leprosy. Early diagnosis through recognition of oral symptoms is critical in preventing irreversible physical and social consequences. Dentists can play a key role in identifying leprosy, particularly when examining patients in endemic regions. **Conclusion:** Oral manifestations of leprosy provide an important diagnostic tool for early detection, potentially preventing severe complications, including physical disability and the associated socio-economic challenges. Dentists should be aware of these symptoms to help improve treatment outcomes and patient quality of life.

§ Corresponding Author
E-mail address: nurfiantieva@gmail.com (Nurfianti)

DOI: 10.32793/jida.v7i2.1279

INTRODUCTION

Morbus Hansen, also known as leprosy, is a chronic infectious disease caused by *Mycobacterium leprae* and *M. lepromatosis*.[1] It remains a significant health concern, particularly in tropical and subtropical regions.[2] The disease primarily affects the peripheral nerves, skin, and other tissues, sparing the central nervous system. In Indonesia, which ranks third globally in leprosy cases, 16,825 new cases were reported in 2013.[3] A study at Bali Mandara Hospital from 2018 to 2020 found that among 55 leprosy patients, 71% were male, with the majority aged 25-44 years and 92.7% having multibacillary type.[4] Genetic factors may influence susceptibility to M. leprae infection, potentially affecting cellular immune responses.[1] Pregnancy can increase the risk of leprosy infection or relapse due to physiological and immunological changes.[3]

Transmission of leprosy is not fully understood, it likely occurs through inhalation of infectious aerosols and direct contact with untreated patients.[5,6] The nose is considered the main transmission route, with multibacillary cases posing a higher risk.[5] Other potential sources include animal reservoirs, particularly armadillos.[5,7] Successful control strategies have included BCG vaccination, active case finding, and multidrug therapy adherence.[5] Treatment typically involves a combination of dapsone, rifampicin, and clofazimine for 6-12 months.[6,7] Early detection and treatment of leprosy are essential to prevent irreversible nerve damage, sensory loss, and disabilities. Prolonged disease progression can result in complications such as peripheral neuropathy, muscle weakness, and neuropathic ulcers, requiring a multidisciplinary approach to management.[7,8]

The appropriate timing for leprosy diagnosis is as early as possible when the initial signs and symptoms appear, such as skin lesions, nerve tenderness, or sensory changes. According to research, the incubation period for *Mycobacterium leprae* ranges from 3 to 10 years, which can delay symptom onset.[9] However, early detection is critical because delayed diagnosis, such as cases identified after 4 months to 4 years, significantly increases the risk of nerve damage, peripheral neuropathy, and associated disabilities. Delayed diagnosis increases the risk of disabilities and deformities, leading to stigmatization and reduced quality of life for patients.[9,10] The disease can affect multiple organs and body structures, with skin signs typically being the first identifiable symptoms.[11] Oral involvement may include lesions on the tongue, lips, hard palate, buccal mucosa, uvula, faucial pillars, and gums. Raising awareness among dental professionals about leprosy's classification, pathogenesis, clinical features, and oral aspects is essential for early detection and improved patient outcomes.[9]

This paper reports on cases of Leprosy disease with oral manifestations that were referred to the Oral Medicine Clinic at Cipto Mangunkusumo Hospital (RSCM)

CASE REPORT

Prior to the examination, all patients provided written informed consent, ensuring their understanding of the procedures, risks, and benefits in compliance with ethical standards. The following Table 1-4 presents a comparative analysis of five cases of Leprosy Disease (LD) organized in a matrix format to facilitate the evaluation of data and symptoms.

Table 1. Case details

Parameter	Case 1	Case 2	Case 3	Case 4	Case 5
Gender and Age	Male, 55 years	Male, 57 years	Male, 27 years	Male, 49 years	Female, 23 years
Type of LD	Borderline Lepromatous (BL)	BL with Erythema Nodosum Leprosum (ENL)	Lepromatous (LL) with ENL	BL with ENL	BL with ENL
Duration of LD	4 months	4 years	2 years	4 years	1 year
Systemic Conditions	None	Gastritis, Hypertension	None	Diabetes Mellitus, Asthma	Gastritis
LD Therapy	Rifampin, Dapsone, Clofazimine	Clofazimine, Methylprednisolone, Omeprazole, Neurotropic vitamins	Clofazimine, Methylprednisolone, Calcium supplements, Neurotropic vitamins	Methylprednisolone, Calcium Lactate, Neurotropic vitamins	Methylprednisolone, Paracetamol, Ranitidine

Table 2. Skin lesion as manifestation of LD

Parameter	Case 1 (Figure 1)	Case 2 (Figure 2)	Case 3 (Figure 3)	Case 4 (Figure 4)	Case 5 (Figure 5)
Location	Both forearms	Both upper and lower arms	Face, arms, and legs	Face, arms, and legs	Cheeks and both arms
Manifestation	White plaques, non-tender	Multiple erythematous plaques, tender	Dull erythematous macules, tender	Erythematous macules, tender	Multiple erythematous nodules, tender

Table 3. Oral disease manifestation of LD

Parameter	Case 1 (Figure 1)	Case 2 (Figure 2)	Case 3 (Figure 3)	Case 4 (Figure 4)	Case 5 (Figure 5)
Location	Lips, tongue, buccal mucosa, gingiva, periodontal area	Dry lips, labial mucosa, gingiva, periodontal area	Dry lips, buccal mucosa, gingiva	Dry lips, fissures at the mouth corners, gingiva	Dry lips, labial mucosa, gingival
Manifestation	- White Lesion - Tongue Atrophy - Gingivitis - Periodontitis - Ulceration	- White Lesion - Tongue Atrophy - Gingivitis - Periodontitis - Ulceration	- White Lesion - Tongue Atrophy - Gingivitis	- White Lesion - Tongue Atrophy - Gingivitis - Angular cheilitis	- White Lesion - Ulceration

Table 4. Other oral health issues

Parameter	Case 1 (Figure 1)	Case 2 (Figure 2)	Case 3 (Figure 3)	Case 4 (Figure 4)	Case 5 (Figure 5)
Location	- Chronic gingivitis - Periodontitis - gangrene radix - Pulp irritation	- Traumatic ulcer - Chronic gingivitis - Periodontitis - gangrene radix - Pulp irritation	- Chronic gingivitis - Periodontitis - gangrene radix - Pulp irritation	- Angular cheilitis - Chronic gingivitis - gangrene radix - Pulp irritation	- Cheilosis - Traumatic ulcer - Chronic gingivitis - gangrene radix - Pulp irritation

DISCUSSION

The case reports presented illustrate various extraoral and oral manifestations of Leprosy disease, highlighting the diversity in clinical presentations.[12,13] The extraoral manifestations of leprosy disease vary according to the type or classification of the disease. The classification system for leprosy disease was first established in 1960 by Ridley and Jopling, and it categorizes the disease into six classes based on histological appearance and severity. These classes are: Indeterminate (I), Tuberculoid (TT), Borderline Tuberculoid (BT), Mid-Borderline (BB), Borderline Lepromatous (BL), Lepromatous (LL).[12] This classification system is widely used because it aligns with clinical, immunological, and pathological findings, and is correlated with the number of acid-fast bacilli present in the dermis.[13] This correlation is expressed through the Bacteriological Index (BI), which ranges from 0 to 6. The BI helps determine the intensity of antimicrobial therapy and the likelihood of reactional states, as well as the dominance of either Th1 or Th2 lymphocyte responses.[13]

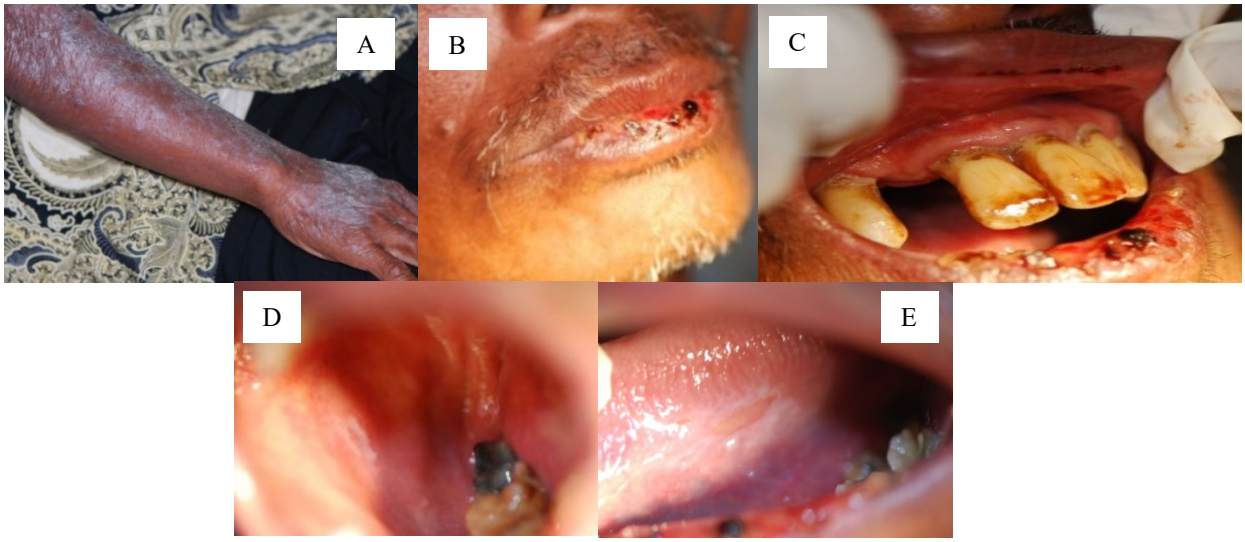

Figure 1: (A) White plaques on both forearms. (B) Erosion and dark reddish crusts. (C) Poor oral hygiene with subgingival and supragingival calculus. (D) White lesion on the right buccal mucosa. (E) Ulcer with a red base and white margins, measuring 10x3 mm, on the left ventral surface of the tongue.

The increasing severity of leprosy disease types, progressing from Indeterminate (I), Tuberculoid (TT), Borderline Tuberculoid (BT), Mid-Borderline (BB), Borderline Lepromatous (BL), to Lepromatous (LL), is primarily attributed to the declining immune response mediated by Th1 lymphocytes and the increasing dominance of Th2 lymphocyte activity, which correlates with higher bacterial loads in the dermis and systemic tissues.[12,13]

In 1982, the World Health Organization (WHO) developed a simplified classification system for Leprosy disease to facilitate field-based treatment. This classification system divides leprosy disease into two types: Paucibacillary (PB) and Multibacillary (MB). Paucibacillary (PB) Type includes: Indeterminate, Tuberculoid and Borderline Tuberculoid. Multibacillary (MB) Type includes Mid-Borderline, Borderline Lepromatous, Lepromatous. According to WHO recommendations, treatment for MB type originally required a minimum of two years or until skin smears became acid-fast bacilli negative. However, this duration has been reduced to one year. The current regimen for MB type includes daily administration of Dapsone (100 mg) and Clofazimine (50 mg), along with monthly doses of Rifampicin (600 mg) and Clofazimine (300 mg). For PB type, the treatment duration is six months, consisting of daily Dapsone (100 mg) and monthly Rifampicin (600 mg).[14,15]

The first publication addressing oral manifestations of Leprosy disease, with a focus on the correlation between nasal and oral lesions, was by Pavloff in 1930. In 1939, a study was conducted on 456 patients with lepromatous, revealing the following oral manifestations: lesions on the hard palate in 11.7% of cases, soft palate lesions in 5.9%, uvular lesions in 3.2%, lip lesions in 2.09%, and tongue lesions in 1.4%. Oral lesions in leprosy disease typically present as ulcers, nodules, hypopigmentation, or atrophy, often asymptomatic and developing slowly. The soft palate is the most commonly reported site for oral leprosy disease lesions. These lesions can vary, presenting as infiltrations, ulcers, perforations, or yellowish to reddish nodules, which may be sessile or pedunculated, and range in size from 2 to 10 mm. Some nodules may coalesce and are prone to ulceration.[16,17]

Oral manifestation Leprosy disease on the tongue occur in approximately 17% to 25% of cases, typically located on the dorsum, particularly in the anterior two-thirds of the tongue. Clinically, these lesions may present as erosions, atrophy of papillae, fissures, or infiltrated nodules, which can create a "paving stone appearance." Scarring may also occur. In extreme cases, the uvula can be involved, showing signs of fibrosis with partial or complete loss of the uvula. Lesions may also affect the lips, potentially resulting in macrocheilia or microstomia. The gingiva can develop lesions, particularly in the area behind the upper incisors, often associated with lesions on the hard palate. Chronic gingivitis, periodontitis, and periodontoclasia are also common.[17,18]

Oral manifestations of leprosy frequently involve sensory and motor disturbances, resulting in hyperesthesia, paresthesia, and anesthesia in the face, lips, hard palate, tongue, cheeks, and gingiva.[19] As the disease progresses, these oral manifestations become more pronounced with the duration of the illness. A study that examined 172 leprosy patients, found that oral manifestations were present in 2.33% of patients with a disease duration of 0-5 years, 14.53% with a duration of 5-10 years, 6.39% with a duration of 10-15 years, and 6.39% with a duration of 15-20 years. However, this study's findings were less significant both qualitatively and quantitatively due to a large proportion of patients having undergone treatment, while fewer patients had not received treatment. [20]

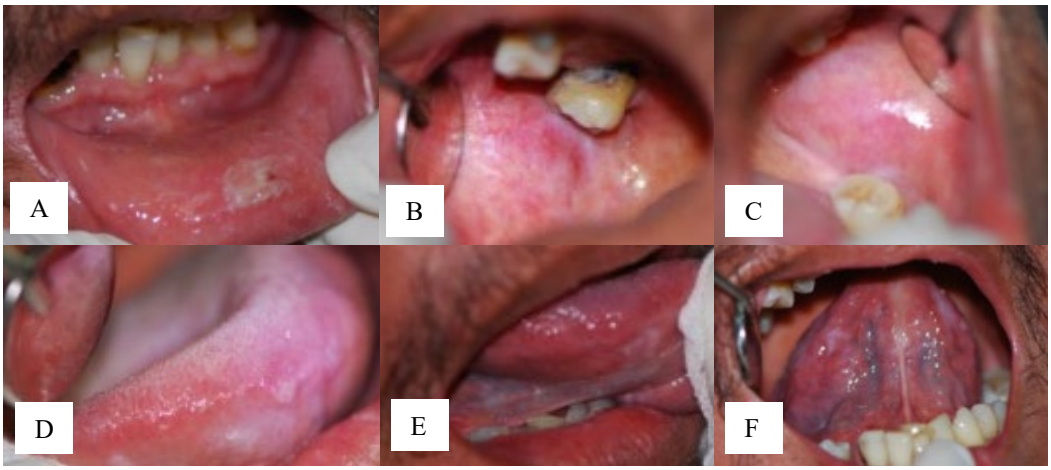

Figure 2: (A) Irregular ulcer on the lower labial mucosa in the region of tooth 41, measuring 12x5 mm. (B) White area on the buccal mucosa in the region of tooth 18. (C) Whitish on the buccal mucosa in the region of tooth 38. (D, E, F) White lesion on the ventral surface of the tongue.

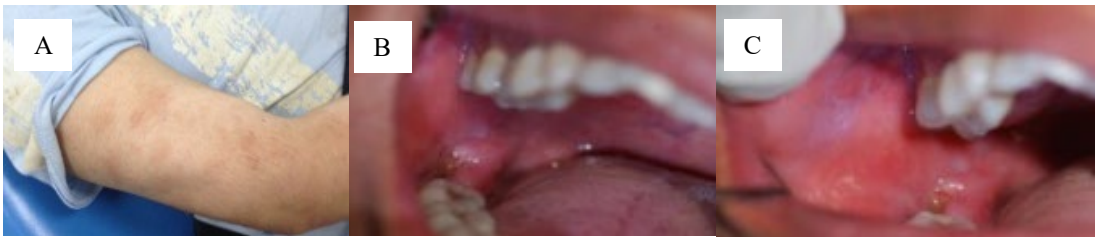

Figure 3: (A) Faint erythematous macule on the arm. (B) White lesion on the right retromolar pad. (C) Erosive area with desquamated epithelial edges on the right buccal mucosa.

Oral lesions in leprosy typically occur in the later stages of the disease. The upper respiratory tract serves as the entry point for the bacteria, making oral lesions secondary as the oral cavity becomes contaminated with bacteria from rhino pharyngeal secretions. Oral lesions are often more severe than nasal lesions because *M. leprae* requires a lower temperature for multiplication. The optimal temperature for survival and proliferation of *M. leprae* is between 27°C and 30°C. This fact clarifies the pathophysiological mechanism behind oral lesions. In a study conducted by Anton Scheepers in 1997, temperatures at 44 WHO-defined topographic sites were found to be below 33.8°C, except for the anterior palate, which had a temperature of 27.4°C. This temperature range was associated with 75.7% of oral leprosy manifestations.[17,21,22]

Mycobacterium leprae attacks Schwann cells (SS), which are part of the peripheral nervous system, by specifically binding to the G-domain located on the laminin-α2 chain of the axon, causing injury, demyelination, and nerve damage. The phagocytosis of *M. leprae* is initially carried out by macrophages. However, macrophages from tuberculoid and lepromatous patients may be inefficient in recognizing certain mycobacterial antigens. Cellular hypersensitivity depends on specific T lymphocytes associated with macrophages responsible for the infection of *M. leprae*.[23,24] CD4 and CD8 T cells, along with cytokines, are crucial in responding to *M. leprae*. CD4 T cells produce a Th1 cytokine pattern, including IFN-γ, which is predominantly seen in lepromatous lesions. In contrast, CD8 T cells in the tuberculoid type produce a Th2 cytokine pattern, including IL-4. Therefore, an individual's susceptibility to leprosy is significantly influenced by their immune system.[25,26]

The imbalance between the immune system and *M. leprae* can lead to leprosy reactions, which are acute episodes affecting the skin and nerves. These reactions can cause morbidity and neurological disabilities and may occur during the disease, during treatment, or after the treatment has concluded.[27,28] Leprosy reactions are classified into two types: Type 1 and Type 2. Type 1, known as Reversal Reaction (RR), is due to a delayed-type hypersensitivity reaction (Type IV) and occurs in borderline patients (BT, BB, and BL). This reaction is associated with cellular immune responses, characterized by the infiltration of IFN-γ and TNF, which are secreted by CD4+ cells at skin and nerve lesions. This results in painful edema and inflammation. Type 1 is marked by skin lesions presenting as edema and erythema, formation of new skin lesions, neuritis, and loss of sensory and motor function in the hands, feet, and face. [27-29]

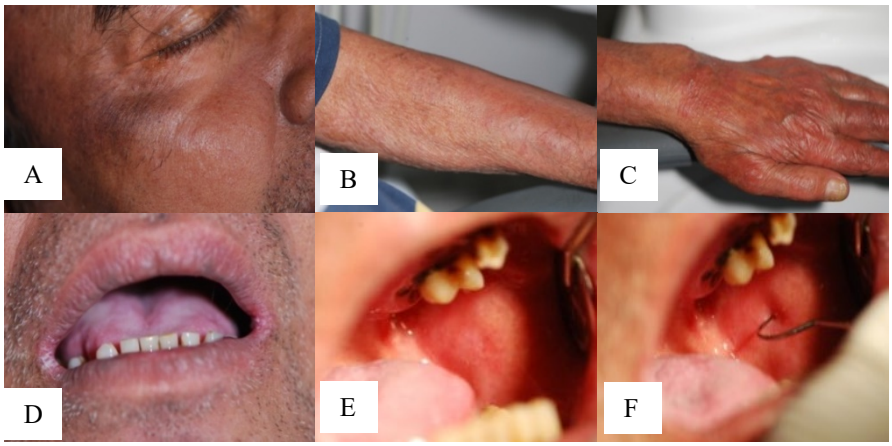

Figure 4: (A, B, C) Erythematous macules on the face and arm. (D) Fissures at the right and left corners of the mouth. (E) White lesion accompanied by an erosive area on the left buccal mucosa. (F) No pain upon probing.

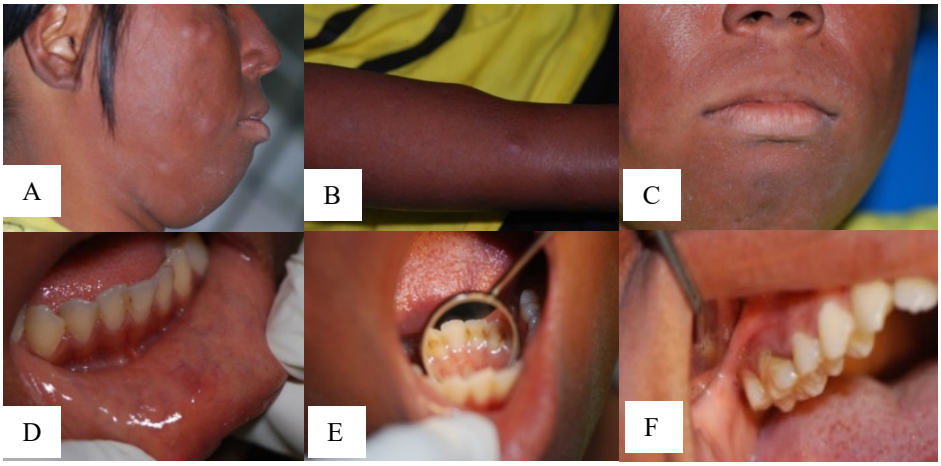

Figure 5: (A, B, C) Multiple erythematous nodules, painful on pressure. (D) Healing ulcer on the lower labial mucosa in region 31, with a white base and red edges, diameter 0.5 mm. (E, F) Poor oral hygiene with subgingival and supragingival calculus.

Type 2 reactions, known as Erythema Nodosum Leprosum (ENL), are a result of a delayed-type hypersensitivity reaction (Type III). This type is associated with the humoral immune system and occurs due to substances released by destroyed mycobacteria, leading to immune complex deposition in tissues. ENL occurs only in the BL and LL forms of leprosy. It is characterized by target lesions of erythema multiforme that can appear anywhere on the body, accompanied by symptoms such as fever, malaise, myalgia, edema, arthralgia, lymphadenopathy, and systemic involvement, including potential liver or kidney damage.[30,31]

This report highlights the variations in skin and oral lesions associated with leprosy, which aid in diagnosis alongside a thorough medical history. While the literature frequently notes lesions on the palate, they were not observed in this report, likely because the patients had already received treatment, leading to better disease control. In one case, the presence of erythema multiforme was suspected to be a hypersensitivity reaction to rifampicin, dapsone, and clofazimine. Oral manifestations of leprosy were observed in all five cases, with gingivitis accompanied by poor oral hygiene being a common finding. Periodontitis was present in two cases. Oral ulcerations were noted in three cases, with one case involving an ulcer accompanied by anesthesia. Erosive areas with desquamating epithelial borders and anesthesia were found in three cases. Hypopigmented lesions with anesthesia were present in three cases as well. Oral manifestations of leprosy on the tongue, including fissures and atrophy, were observed in two cases. Angular cheilitis was identified in one leprosy patient with systemic diabetes mellitus.

CONCLUSION

It is important to remember that Leprosy Disease remains a persistent infection that has not been fully eradicated, with Indonesia still facing endemic regions where this health issue persists. The soft tissues of the oral cavity can be a site of leprosy manifestations, making it crucial for dentists to recognize oral lesions associated with the disease. Early detection and diagnosis of leprosy in undiagnosed patients can expedite treatment, preventing physical disabilities that could have significant socio-economic impacts, as well as reducing the stigma and discrimination faced by those with the disease. Furthermore, dentists play a vital role in maintaining the quality of life for patients through the preservation of oral health and hygiene.

ACKNOWLEDGMENT

We would like to express our sincere gratitude to Dr. Cipto Mangunkusumo Hospital for their assistance in case referrals and clinical data collection. We also extend our appreciation to all patients who participated in this research, without whom this study would not have been possible. Finally, we acknowledge the invaluable contributions of our colleagues and advisors for their insightful feedback and guidance throughout the research process.

PATIENT CONSENT STATEMENT

All patients that participated in this study had provided written informed consent at Oral Medicine Clinic at Cipto Mangunkusumo Hospital (RSCM).

REFERENCE

1. Gofur, N. R. P., Gofur, A. R. P., Soesilaningtyas, G. R., KaLDina, M., & Putri, H. M. (2021). Genes associated as risk factor morbus Han-sen's Disease: A review article. J Clin Images Med Case Rep, 2(2), 1021.
2. Idris, F., & Mellaratna, W. P. (2023). Morbus Hansen (Kusta). GALENICAL: Jurnal Kedokteran dan Kesehatan Mahasiswa Malikussaleh, 2(6), 11-23.
3. Widasmara, D., Basuki, S., Florensia, D., Setyagraha, A., & Prasetyorini, N. (2020). Efektivitas multi drug therapy pada transmisi morbus hansen transplasental. Intisari Sains Medis, 11(2), 425-428.
4. Aviana, F., Birawan, I. M., & Sutrini, N. N. A. (2022). Profil Penderita Morbus Hansen di Poliklinik Kulit dan Kelamin RSUD Bali Mandara Januari 2018-Desember 2020. Cermin Dunia Kedokteran, 49(2), 66-68.
5. Hambridge, T., Nanjan Chandran, S. L., Geluk, A., Saunderson, P., & Richardus, J. H. (2021). Mycobacterium leprae transmission characteristics during the declining stages of leprosy incidence: a systematic review. PLoS neglected tropical diseases, 15(5), e0009436.
6. Andrew, K., & Kadala, M. (2020). Leprosy: A Review of History, Clinical Presentation and Treatments. American Journal of Infectious Diseases, 8(3), 88-94.
7. Le, P. H., Philippeaux, S., Mccollins, T., Besong, C., Kellar, A., Klapper, V. G., & Kaye, A. D. (2023). Pathogenesis, clinical considerations, and treatments: A narrative review on leprosy. Cureus, 15(12).
8. Bento, L. F. D. A., Brandão, D. G., Ferreira, K. D. M., Santana, S. F., Silva, L. K. D. O., Dos Santos, E. G. F., & Neto, J. D. A. L. (2020). Leprosy Lesions in Oral Cavity: A Review Of The Literature On Aspects Relevant To The Dentist. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 130(3), e284.
9. Singh, M., Sawhney, H., Mishra, R., & Kumar, J. (2022). An overview of leprosy with its oral manifestations: A comprehensive review. SRM Journal of Research in Dental Sciences, 13(4), 185-189.
10. Ferreira, I. S., & Ribeiro, A. Z. L. (2021). Prejuízos do Diagnóstico Tardio em Hanseníase: Uma Revisão Integrativa. Revista de Patologia do Tocantins, 8(2), 65-69.
11. Makhakhe, L. (2021). Leprosy review. South African Family Practice, 63(4).
12. Gilmore, A., Roller, J., & Dyer, J. A. (2023). Leprosy (Hansen's disease): an update and review. Missouri Medicine, 120(1), 39.
13. Bhandari, J., Awais, M., & Gupta, V. (2020). Leprosy (Hansen Disease). StatPearls.
14. Margoles, L., del Rio, C., & Franco-Paredes, C. (2011). Leprosy: a modern assessment of an ancient neglected disease. Boletín Médico del Hospital Infantil de México, 68(2), 110-116.
15. Borah Slater, K. (2023). A Current Perspective on Leprosy (Hansen's Disease). In Vaccines for Neglected Pathogens: Strategies, Achievements and Challenges: Focus on Leprosy, Leishmaniasis, Melioidosis and Tuberculosis (pp. 29-46). Cham: Springer International Publishing.
16. Vohra, P. (2022). Oral and systemic manifestations in leprosy a hospital-based study with literature review. Indian Journal of Dermatology, 67(6), 631-638.
17. Vohra, P., Rahman, M. S. U., Subhada, B., Tiwari, R. V. C., Althaf, M. N., & Gahlawat, M. (2019). Oral manifestation in leprosy: a cross-sectional study of 100 cases with literature review. Journal of Family Medicine and Primary Care, 8(11), 3689-3694.

18. Mezaiko, E., Silva, L. R., Prudente, T. P., de Freitas Silva, B. S., & Silva, F. P. Y. (2023). Prevalence of oral manifestations of leprosy: a systematic review and meta-analysis. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology.
19. Ebenezer, G. J., & Scollard, D. M. (2021). Treatment and evaluation advances in leprosy neuropathy. Neurotherapeutics, 18(4), 2337-2350.
20. Thirugnanasambandan TS, Latha S, Kumar MS. Clinical and Pathological Evaluation of Oral. Indian J Multidiscip Dent. 2011;1(2):105–9.
21. Castellano, G. M., Villarroel-Dorrego, M., & Lessmann, L. C. (2020). Characteristics of oral lesions in patients with Hansen disease. Actas Dermo-Sifiliográficas (English Edition), 111(8), 671-677.
22. Scheepers A. Correlation of Oral Surface Temperatures and the Lesions of Leprosy '. Int JournaI Lepr. 1970;66(2):214–7.
23. Brügger, L.M., dos Santos, M.M., Lara, F.A., & Mietto, B.D. (2023). What happens when Schwann cells are exposed to Mycobacterium leprae – A systematic review. IBRO Neuroscience Reports, 15, 11 - 16.
24. Santos, R.G., Nunes, B.V., Domiciano, G.S., Santos, H.G., Silva, J.C., Martins, M.D., Delfino, P.H., & Mesquita Júnior, F. (2021). Leprosy: a view of the molecular interaction of Mycobacterium leprae with Schwann Cells. São Paulo Medical Journal.
25. Yasmin, H., Varghese, P.M., Bhakta, S., & Kishore, U. (2021). Pathogenesis and Host Immune Response in Leprosy. Advances in experimental medicine and biology, 1313, 155-177 .
26. Marçal, P.H., Gama, R.S., Pereira de Oliveira, L.B., Martins-Filho, O.A., Pinheiro, R.O., Sarno, E.N., Moraes, M.O., & de Oliveira Fraga, L.A. (2020). Functional biomarker signatures of circulating T-cells and its association with distinct clinical status of leprosy patients and their respective household contacts. Infectious Diseases of Poverty, 9.
27. Dewi, D.A., Djatmiko, C.B., Rachmawati, I., Arkania, N., Wiliantari, N.M., & Nadhira, F. (2023). Immunopathogenesis of Type 1 and Type 2 Leprosy Reaction: An Update Review. Cureus, 15.
28. Luo, Y., Kiriya, M., Tanigawa, K., Kawashima, A., Nakamura, Y., Ishii, N., & Suzuki, K. (2021). Host-related laboratory parameters for leprosy reactions. Frontiers in Medicine, 8, 694376.
29. Jha, A.K., Zeeshan, M., Tiwary, P.K., Singh, A., Roy, P.K., & Chaudhary, R.K. (2020). Dermoscopy of Type 1 Lepra Reaction in Skin of Color. Dermatology Practical & Conceptual, 10.
30. Mas Rusyati, L.M., Hatta, M., Widiana, I.G., Adiguna, M.S., Wardana, M., Dwiyanti, R., Noviyanti, R.A., Sabir, M.M., Yasir, Y., Paramita, S., Junita, A.R., & Primaguna, M.R. (2020). Higher Treg FoxP3 and TGF-β mRNA Expression in Type 2 Reaction ENL (Erythema Nodosum Leprosum) Patients in Mycobacterium leprae Infection. The Open Microbiology Journal.
31. Abril-Pérez, C., Palacios-Diaz, R.D., Navarro-Mira, M.Á., & Botella-Estrada, R. (2021). Successful treatment of erythema nodosum leprosum with apremilast. Dermatologic Therapy, 35.