A Case Report of Unrecognized Lepromatous Leprosy Occurring in Conjunction with Pemphigus Vulgaris

Supattra Chardleelahar MD*, Tanaporn Borriboon MD*, Pinnaree Kattipathanapong MD*, Poonnawis Sudtikoonaseth MD*, Wanida Limpongsanurak MD.**

** Institute of Dermatology, Department of Medical Services, Ministry of Public Health, Bangkok, Thailand.*
***Queen Sirikit National Institute of Child Health, Department of Medical Services, Thailand.*

ABSTRACT:
Leprosy is a chronic, infectious disease of a significant public health concern, primarily affecting the skin and peripheral nerves. The causative agent of this disease is *Mycobacterium leprae*, and despite its recognition as an ancient affliction, it continues to be occasionally encountered in the southern regions of Thailand. The manifestation and progression of leprosy are known to be influenced by the host's genetic background and immune response. We present a case of a 45-year-old Thai male who developed new infiltrative papules and nodules while undergoing oral immunosuppressive therapy for the treatment of his underlying pemphigus vulgaris condition. Upon histopathological examination, the presence of histiocytes containing abundant acid-fast bacilli was observed. The patient was successfully treated through a 2-year course of multidrug therapy. This case highlights the challenges in diagnosing leprosy in immunocompromised individuals and underscores the importance of vigilant recognition of the disease by healthcare practitioners. It is imperative that medical professionals remain aware of the potential for leprosy to present in unexpected ways and take necessary steps to diagnose and treat the disease effectively.
Key words: Lepromatous leprosy, Pemphigus vulgaris, Oral immunosuppressive agents

Introduction

Leprosy, clinically referred to as Hansen disease, is a chronic granulomatous infection caused by *Mycobacterium leprae*. The bacillus displays low virulence and pathogenicity, resulting in a prolonged incubation period. The disease primarily affects the skin and peripheral nervous system, leading to various cutaneous manifestations and peripheral neuropathy. In this case report, we present a patient with a pre-existing condition of severe pemphigus vulgaris who was receiving systemic immunosuppressive therapy and subsequently developed lepromatous leprosy, a subtype of the disease characterized by diffuse cutaneous involvement and high bacterial load.

Case report

A 45-year-old male has been diagnosed with severe pemphigus vulgaris since 2015, confirmed by skin biopsy. He is in partial remission. The current immunosuppressive therapy consists of azathioprine 100 mg/day and prednisolone 10 mg/day. During the follow-up period in July 2020, the patient progressively developed multiple painless, non-swelling, erythematous papules on the extremities for two months. He denied any history of close contact with the lepromatous patient. He had normal sweating and visual acuity but did not have a

Corresponding Author: Tanaporn Borriboon MD, email : tanaporn.borriboon@gmail.com

Received: 14 February 2023 Revised: 24 May 2023 Accepted: 29 May 2023

fever, paresthesia, arthralgia, scrotal swelling, and tenderness. Topical corticosteroids were initially prescribed without clinical improvement. However, the lesions gradually increased in number and size and spread to the abdomen, back, and chest wall. The skin examination revealed multiple non-scaly infiltrative erythematous papules and nodules on the chest wall. (Figure 1). No tenderness or swelling was observed. Neurological examination revealed normal pain, temperature, and touch sensation. The patient has no wrist drop or foot drop. The physician initially suspected pseudolymphoma, cutaneous lymphoma, lymphomatoid papulosis in the differential diagnosis. As a result, a skin biopsy of skin lesions from the right forearm and abdomen was performed. Histopathologic examination revealed nodular infiltration predominately of foamy histiocytes admixed with few neutrophils and nuclear dusts, lymphocytes, and plasma cells surrounding the superficial and deep vascular plexus and periadnexal area. In addition, the acid-fast stain was positive. (Figure 2). Slit skin smear from both earlobes and the skin lesions demonstrated a bacteriological index of 2+ to 3+. Laboratory investigation to detect other systemic involvement of leprosy reaction showed no abnormal finding. The patient was finally diagnosed with lepromatous leprosy with erythema nodosum leprosum. Although the clinical manifestation of leprosy reaction in this case is obscured due to current immunosuppressive medication. The treatment with multidrug therapy, consisting of monthly doses of rifampicin 600 mg and clofazimine 300 mg, daily doses of dapsone 100 mg, and clofazimine 50 mg were initiated. And the concurrent treatment of his underlying pemphigus vulgaris was well-controlled with azathioprine 50-100 mg/day and prednisolone 10-20 mg/day. There was no disease flare during the leprosy treatment. The skin lesions had disappeared completely and the patient has no neurodeficit after two years of treatment.

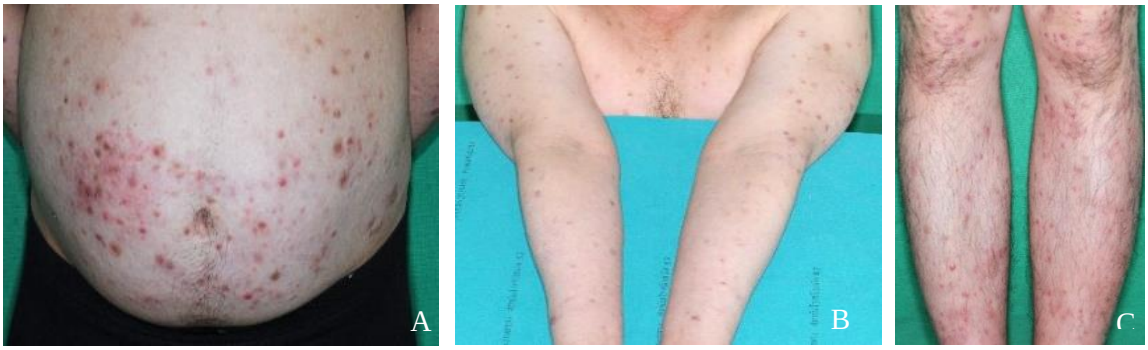

Figure 1 Multiple non-scaly infiltrative erythematous papules on the abdominal wall (A) both arms (B) and legs (C)

Discussion

Leprosy, also known as Hansen's disease, is a chronic infectious disease caused by *Mycobacterium leprae*[1]. The disease primarily affects the cutaneous and peripheral nervous systems and the mucosal membranes of the upper respiratory tract and eyes[2]. The persistence of the infection and the slow progression of symptoms characterizes the disease.

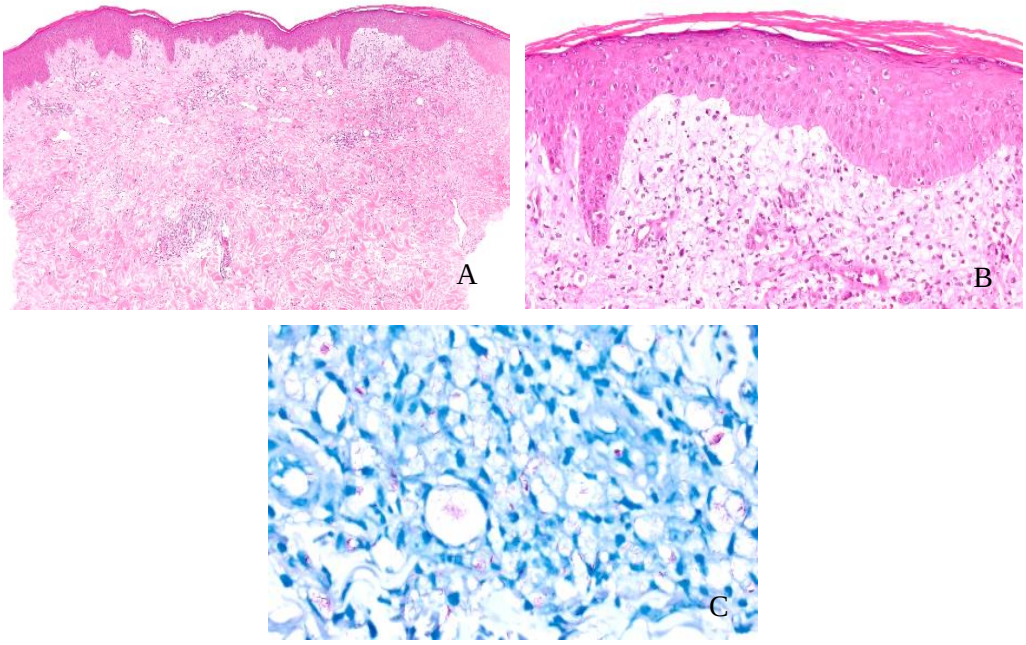

Figure 2 Histopathological findings revealed diffuse dermal infiltrate with foamy histiocytes, neutrophils and nuclear dusts. Numerous acid-fast bacilli were detected. (Hematoxylin-eosin stain; original magnifications: A, X4 and B, X40, Ziehl Neelsen stain; original magnification: C, X60)

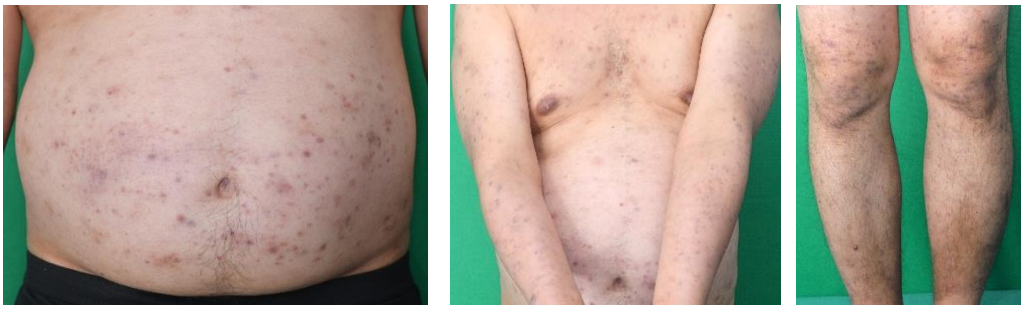

Figure 3 After completion of 2-year WHO multidrug therapy.

The clinical presentation of leprosy is influenced by both innate and adaptive immunity. However, the adaptive immune system is more closely associated with the characteristic spectrum of leprosy. The defining feature of lepromatous leprosy (LL) patients is the presence of *M. leprae*-specific T cell anergy and dissemination of the bacilli. This highlights the crucial role the adaptive immune system plays in the manifestation of the disease[3-5]. The manifestation of leprosy is strongly influenced by the interactions between the host and the pathogen. The susceptibility of an individual to develop leprosy is highly variable and determined by multiple factors. Some key contributors to susceptibility include close contact with a recently diagnosed patient, particularly those with polar lepromatous leprosy, and conditions that result in immunosuppression or immunodeficiency[6-8]. In

addition to the study by Umar et al., a case of a Taiwanese renal transplant recipient who was concomitantly infected with borderline lepromatous leprosy three years post-transplantation. The patient had received immunosuppressive therapy, including oral prednisolone, tacrolimus, and mycophenolate, as part of their post-transplant management. This serves as evidence of the role that immunosuppression can play in increasing the susceptibility of individuals to leprosy[8]. Additionally, the findings from the studies emphasized the significance of further investigating the interplay between immunosuppression and leprosy. Such studies would contribute to advancing of our understanding of the complex relationships between these factors. They may inform the development of more efficacious and precise therapeutic approaches for individuals with leprosy, especially those who exhibit impaired immunity due to medical conditions or treatment regimens[9]. Consistent with the prior literature, the systematic review and meta-analysis performed by Barroso et al. presents further information regarding the incidence of leprosy in individuals with suppressed immunity resulting from rheumatologic, dermatologic, and gastroenterological diseases. The review disclosed a considerable disparity in the incidence of leprosy, with values ranging from 0.13 to 116.18 cases per 100,000 patients/year in the United States and Brazil, respectively. The meta-analysis further revealed that the incidence of leprosy in immunosuppressed patients with rheumatic diseases was 0.00084[10]. These findings underscore the need for continuous observation and surveillance for leprosy in individuals with compromised immunity as a result of medical conditions or therapeutic interventions. In the context of individuals with pemphigus undergoing immunosuppressive treatment, it is crucial to consider the elevated risk of contracting opportunistic infections. A study has documented that the incidence of opportunistic infections within the first year after the diagnosis of pemphigus was determined to be 9.3%, which decreased over time[9]. Advanced age and the presence of diabetes were identified as potential risk factors for developing these infections. The spectrum of identified infectious agents included nocardia, cytomegalovirus, legionella, and listeria. These findings highlight the significance of ongoing surveillance and implementation of preventative measures in individuals with pemphigus receiving immunosuppressive treatments. High-dose azathioprine therapy, frequently used in clinical practice, has been documented to cause myelosuppression as an adverse side effect. Furthermore, the administration of glucocorticoids, including prednisolone, has been shown to exert a marked suppressive impact on the function of various immune cells, including monocytes, lymphocytes, and Th1 and Th2 cells[10]. This immunosuppressive effect is considered more pronounced than its impact on polymorphonuclear leukocyte function. Given the crucial role of the immune system in combating infections, the prolonged utilization of glucocorticoids may exacerbate and relapse granulomatous infectious diseases, such as tuberculosis. These findings emphasize the importance of carefully monitoring and managing patients receiving immunosuppressive treatments. In this case report, a patient presenting with pemphigus vulgaris, who underwent long-term treatment with prednisolone and azathioprine for five years developed a new onset of multiple, non-scaly, infiltrative erythematous papules on the trunk and extremities. Initially, the treating physician did not consider leprosy in a differential diagnosis until a skin biopsy was performed and the histopathological findings revealed evidence of leprosy. The diagnosis of leprosy can pose a challenge for medical practitioners due to its varied clinical

manifestations and multiple subtypes. Therefore, physicians need to maintain a heightened level of clinical suspicion for underlying medical conditions when patients receiving immunosuppressive therapy present with new cutaneous lesions. This case report presents a rare occurrence of concomitant lepromatous leprosy and pemphigus vulgaris in a single patient, resulting from azathioprine-induced immunosuppression, and is the first recorded instance of such simultaneous presentation in the literature.

References

1. Maymone MB, Laughter M, Venkatesh S, et al. Leprosy: Clinical aspects and diagnostic techniques J Am Acad Dermatol 2020;83:1-14.
2. Nath I, Saini C, Valluri VL. Immunology of leprosy and diagnostic challenges. Clin in Dermatol 2015;33:90-8.
3. Reibel F, Cambau E, Aubry A. Update on the epidemiology, diagnosis, and treatment of leprosy. Med Mal Infect 2015;45:383-93.
4. Sadhu S, Mitra DK. Emerging Concepts of Adaptive Immunity in Leprosy. Front Immunol 2018;9:604.
5. da Silva MB, Portela JM, Li W, et al. Evidence of zoonotic leprosy in Pará, Brazilian Amazon, and risks associated with human contact or consumption of armadillos. PLoS Negl Trop Dis 2018;12:e0006532.
6. Moet FJ, Pahan D, Schuring RP, Oskam L, Richardus JH. Physical distance, genetic relationship, age, and leprosy classification are independent risk factors for leprosy in contacts of patients with leprosy. J Infect Dis 20061;193:346-53.
7. Trindade MAB, Palermo MdL, Pagliari C, et al. Leprosy in transplant recipients: report of a case after liver transplantation and review of the literature. Transpl Infect Dis 2011;13:63-9.
8. Aarestrup FM, Sampaio EP, de Moraes MO, Albuquerque EC, Castro AP, Sarno EN. Experimental Mycobacterium leprae infection in BALB/c mice: effect of BCG administration on TNF-alpha production and granuloma development. Int J Lepr Other Mycobact Dis 2000;68:156-66.
9. Barroso DH, Brandão JG, Andrade ESN, et al. Leprosy detection rate in patients under immunosuppression for the treatment of dermatological, rheumatological, and gastroenterological diseases: a systematic review of the literature and meta-analysis. BMC Infect Dis 2021;21:1-9.
10. Leshem YA, Gdalevich M, Ziv M, David M, Hodak E, Mimouni D. Opportunistic infections in patients with pemphigus. J Am Acad Dermatol 2014;71:284-92.