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CASE REPORTS ON LEPROSY:
A SHARED PRACTICE

Concomitance of lepromatous leprosy and squamous cell carcinoma: case report

Concomitância da hanseníase virchowiana e carcinoma de células escamosas: relato de caso

Concomitancia entre lepra lepromatosa y carcinoma de células escamosas: reporte de caso

Hugo Hatanaka[1], *Bruno de Carvalho Dornelas*[1], *Pauline Dias Soares Girardi*[1], *Caio Oliveira Sena*[1], *Marcelo Campos Rocha*[1], *Isabela Maria Bernardes Goulart*[2]

[1] Federal University of Uberlândia, Clinical Hospital, Pathological Anatomy Unit, Uberlândia, Minas Gerais (MG), Brazil.
[2] Federal University of Uberlândia, Clinical Hospital, National Reference Center for Sanitary Dermatology and Leprosy, Uberlândia, Minas Gerais (MG), Brazil.

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CONTACT INFORMATION:
Bruno de Carvalho Dornelas
Federal University of Uberlândia
E-mail: bruno.dornelas@ufu.br

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ABSTRACT

Introduction: leprosy is an endemic disease in Brazil, ranking second worldwide for the number of new cases diagnosed yearly. However, late diagnosis of this disease is still common. **Objective:** to alert health professionals to the importance of recognizing the insidious signs of leprosy, both clinical and histopathological, even in the presence of other, more apparent alterations. **Presentation and discussion of the case:** a man with skin lesions suggestive of squamous cell carcinoma. On histological examination, besides the carcinoma, there were aggregates of foamy macrophages full of acid-fast bacilli compatible with lepromatous leprosy. A more detailed physical examination by a multidisciplinary team from a National Reference Center also revealed skin with a

diffuse infiltrated appearance and supraciliary madarosis, alterations not noticed in the first evaluation at another service. **Final considerations:** this case can help clinical professionals and pathologists pay attention to skin alterations that can make it challenging to diagnose leprosy, especially in endemic regions, to enable early diagnosis and reduce the disabilities related to the disease.

Keywords: *Squamous Cell Carcinoma. Lepromatous Leprosy. Mycobacterium leprae. Elderly.*

RESUMO

Introdução: a hanseníase é uma doença endêmica no Brasil, que ocupa a segunda posição de novos casos diagnosticados por ano no mundo. Contudo, o diagnóstico tardio dessa doença ainda é comum. **Objetivo:** alertar os profissionais de saúde sobre a importância de reconhecer os sinais insidiosos da hanseníase, tanto clínicos quanto histopatológicos, mesmo na presença de outras alterações mais evidentes. **Apresentação e discussão do caso:** homem com lesões cutâneas sugestivas de carcinoma de células escamosas. Ao exame histológico, além do carcinoma, observaram-se agregados de macrófagos espumosos repletos de bacilos álcool-ácido resistentes, compatível com hanseníase virchowiana. Um exame físico mais detalhado realizado por uma equipe multidisciplinar de um centro de referência nacional ainda revelou pele com aspecto infiltrado difuso e madarose supraciliar, alterações não percebidas na avaliação inicial em outro serviço. **Considerações finais:** o presente caso pode contribuir com os profissionais da clínica e patologistas sobre a necessidade de atenção a alterações cutâneas que podem dificultar o diagnóstico de hanseníase, principalmente em regiões endêmicas, visando possibilitar um diagnóstico precoce e a redução das incapacidades relacionadas à doença.

Palavras-chave: *Carcinoma de Células Escamosas. Hanseníase Virchowiana. Mycobacterium leprae. Idoso.*

RESUMEN

Introducción: la lepra es una enfermedad endémica en Brasil, con el segundo mayor número de nuevos casos diagnosticados por año en el mundo. Sin embargo, el diagnóstico tardío de esta enfermedad sigue siendo frecuente. **Objetivo:** alertar a los profesionales de salud sobre la importancia de reconocer los síntomas insidiosos de la lepra, tanto clínicos como histopatológicos, incluso en presencia de otras alteraciones más evidentes. **Presentación y discusión del caso:** hombre con lesiones cutáneas sugestivas de carcinoma de células escamosas. En el examen histológico, además del carcinoma, se observaron

agregados de macrófagos espumosos llenos de bacilos ácido-alcohol resistentes, compatibles con lepra lepromatosa. Un examen físico más detallado realizado por un equipo multidisciplinar de un centro de referencia nacional reveló también piel con aspecto infiltrado difuso y madarosis supraciliar, alteraciones no observadas en la primera evaluación en otro servicio. **Consideraciones finales:** este caso puede ayudar a los profesionales clínicos y patólogos a prestar atención a las alteraciones cutáneas que pueden dificultar el diagnóstico de la lepra, especialmente en regiones endémicas, con el objetivo de permitir un diagnóstico precoz y reducir las discapacidades relacionadas con la enfermedad.

Palabras clave: *Carcinoma de Células Escamosas. Lepra Virchowiana. Mycobacterium leprae. Anciano.*

INTRODUCTION

Leprosy is a disease caused by the bacilli *Mycobacterium leprae* and *Mycobacterium lepromatosis*, which primarily affects the skin and peripheral nerves and still presents a significant new-case detection rate in Brazil[1,2]. However, leprosy remains a neglected disease, not only by the general population but also by many healthcare professionals, resulting in delays in diagnosis and an increase in disease-related disabilities[3].

Cutaneous lesions of leprosy represent a major diagnostic challenge, both from a clinical and a pathological standpoint[4,5]. Clinically, leprosy may manifest without significant dermatological findings yet be diagnosed histologically[6,8]. Conversely, histological findings can be subtle or imperceptible in pathology, even when clinical manifestations are evident[9,10].

Squamous cell carcinoma (SCC) is a malignant disease of epidermal keratinocytes that exhibits variable degrees of differentiation and cytological features[11]. Chronic cutaneous lesions associated with leprosy can create a microenvironment conducive to developing SCC[12-14].

We present the case of an elderly patient with a delayed diagnosis of lepromatous leprosy, identified in an excisional biopsy of SCC. This report aims to alert clinicians to the possibility of concomitant leprosy and other dermatologic conditions – of which only one was clinically apparent at first.

CASE PRESENTATION

An 85-year-old man living in a nursing home in a leprosy-endemic area with a history of tobacco use and systemic arterial hypertension.

He presented to the dermatology outpatient clinic of a tertiary hospital in June 2017, complaining of a progressively enlarging vegetative lesion on

the sternal region, with six months of evolution, suggestive of squamous cell carcinoma. On dermatological examination, the lesion measured 5.0 cm, and there was also an erythematous plaque on the upper portion of the right arm, as well as numerous smaller erythematous papules – suggestive of actinic keratosis – on the face and upper limbs. No other abnormalities were noted during the physical examination at that time.

An incisional biopsy of the sternal skin lesion was performed three months after the initial visit, in September 2017, confirming the diagnosis of squamous cell carcinoma. During follow-up, new hyperkeratotic plaque lesions appeared on the middle third of the left forearm, which were biopsied in January 2018. Histopathological examination of four specimens confirmed squamous cell carcinoma (Figure 1A), hypertrophic actinic keratosis, and keratoacanthoma.

However, in addition to the epithelial proliferations, all four specimens exhibited a marked perivascular and interstitial lymphohistiocytic infiltrate (Figures 1B and 1C), both superficial and deep, affecting hair follicles, eccrine glands, arrector pili muscle, and nerve twigs. A search for mycobacteria by Fite–Faraco stain demonstrated numerous acid-fast bacilli (AFB), often forming globi, located within histiocytes, the interstitium, and endothelial cells, with a bacteriological index (BI) of 6+ according to the Ridley–Jopling scale (Figure 1D). The constellation of histopathological findings led to a secondary diagnosis of lepromatous leprosy, which had not been clinically recognized until that moment.

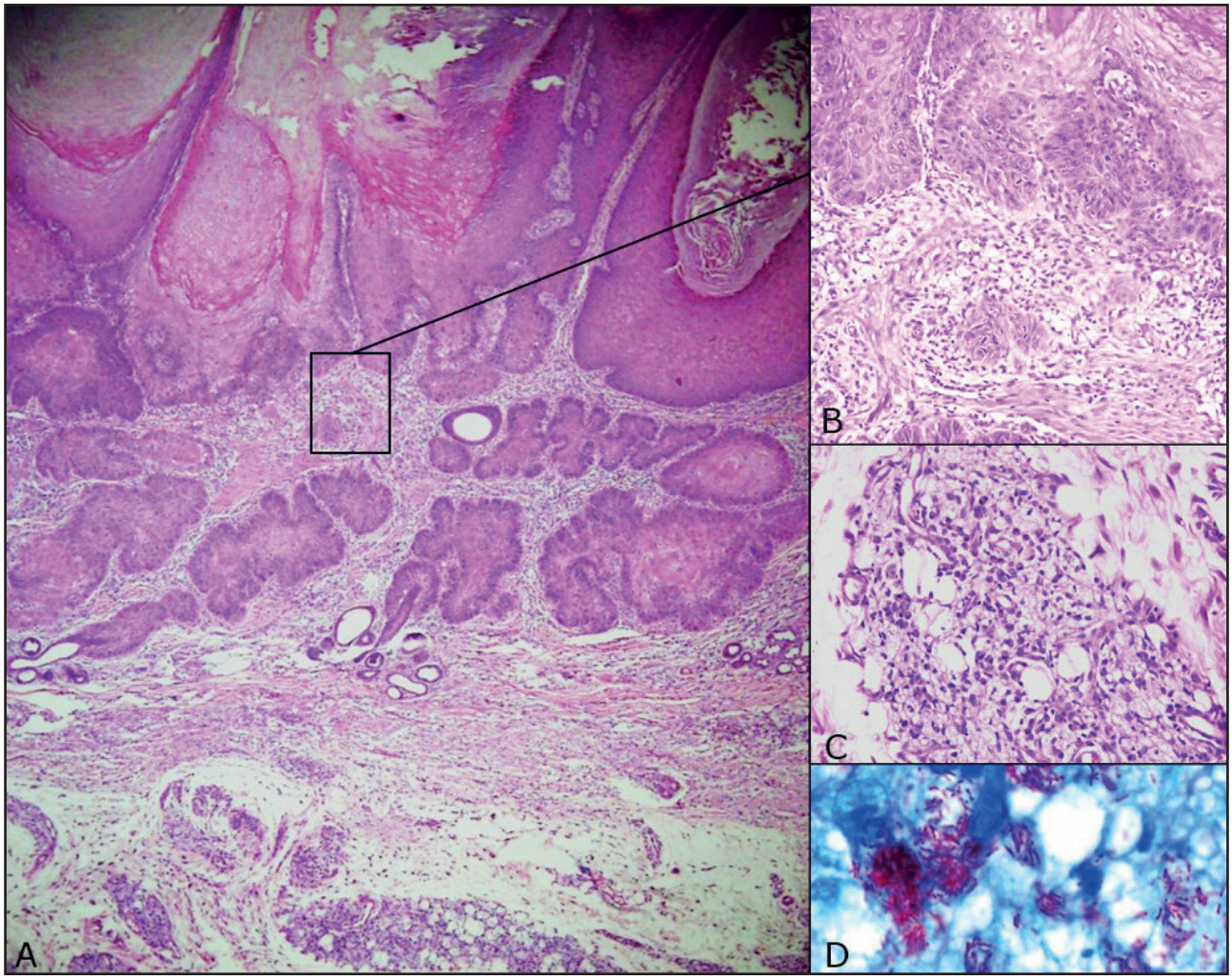
In February 2018, the patient was referred to a National Reference Center for leprosy, where a multidisciplinary team evaluated him. During the assessment, diffuse skin infiltration, supraciliary madarosis, and thickening of the right ulnar and fibular nerves compared to their contralateral counterparts were observed. The degree of physical disability (DPD) was classified as Grade 2 (eyes = 2, hands = 1, feet = 1). Quantitative polymerase chain reaction (qPCR) testing for *Mycobacterium leprae* DNA was positive in both skin samples (CT = 23; load = 3.5×10^8 copies) and dermal scrapings (CT = 27; load = 3.8×10^7 copies).

Treatment with multibacillary multidrug therapy (MDT-MB) was initiated. Still, after one month, it was switched to the ROM regimen, consisting of a monthly supervised dose of rifampicin (600 mg), ofloxacin (400 mg), and minocycline (100 mg), based on a clinical decision due to the patient's anemia and mental confusion.

A skin biopsy performed at the end of treatment, after 24 doses, in March 2020 showed changes consistent with post-treatment regression. The bacteriological index (BI) was 3+, showing only fragmented bacilli. Since the end of treatment, the patient has been monitored periodically, with no signs of active infectious disease.

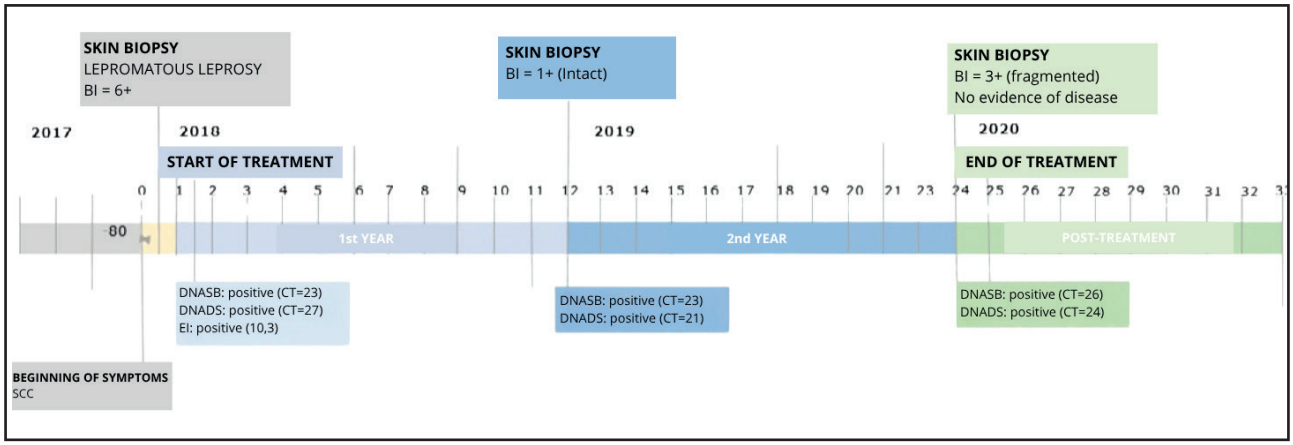
Figure 2 shows the patient's follow-up and the examinations performed during treatment.

Figure 1 – Lepromatous leprosy concomitant with SCC.



Legend: A) In a panoramic view, well-differentiated squamous cell carcinoma (SCC) and collections of foamy macrophages are observed in the dermis (H&E, 2x); B) Aggregates of xanthomatized macrophages and rare lymphocytes are present (H&E, 10x); C) Aggregates of Virchow cells (H&E, 40x); D) Numerous intact and fragmented bacilli forming globi (Fite-Faraco, 40x).
Source: Created by the authors.

Figure 2 – Patient follow-up over time.



Legend: SCC: squamous cell carcinoma; BI: bacteriological index; DNADS: detection of *M. leprae* DNA by qPCR in dermal scraping; EI: ELISA index; DNASB: detection of *M. leprae* DNA by qPCR in skin biopsy.
Source: Created by the author.

DISCUSSION

The correlation between clinical and histological findings obtained through light microscopy is essential for establishing accurate diagnoses, especially dermatopathology. It helps to avoid discrepancies between clinical and histopathological findings[9,15]. Some skin diseases do not present significant clinical changes but can be diagnosed through histology or other diagnostic techniques. In contrast, others may have evident clinical manifestations but absent or very subtle histological changes, which can quickly go unnoticed by the pathologist[5,15,16].

Leprosy is a spectral disease whose manifestations depend on the cell-mediated immune response. Symptoms generally appear gradually and insidiously over the years[17]. Cutaneous manifestations can range from hypopigmented macules or plaques to nodules with an infiltrated appearance[17,18]. Histopathological diagnosis is challenging, especially in indeterminate or early borderline forms, as these present only subtle histological changes. In contrast, other forms of leprosy exhibit more prominent histological alterations, often by identifying the microorganism in greater numbers[15-19].

The diagnostic confirmation of the reported case was obtained through histopathological examination, which revealed numerous foamy histiocytes in the dermis containing a significant number of bacilli, forming globi. Initially, there was no clinical suspicion, and the more typical dermatological changes of leprosy were recognized only by the team at the National Reference Center, which specialized in treating the disease.

It is essential to highlight that various cutaneous changes, often related to photo exposure over the years, can hinder the observation of other characteristic findings of leprosy, especially for professionals not accustomed to evaluating skin diseases[20]. Thus, particularly in the skin of elderly individuals, several changes may be observed, such as the appearance of wrinkles, changes in skin color and thickness, and the presence of various lesions, including hypopigmented plaques and actinic keratoses[21]. This set of alterations can mask or complicate the clinical diagnosis of leprosy or other diseases[5,20-22].

Furthermore, due to the wide variation in neurological and cutaneous signs and symptoms that patients may present, leprosy is considered a great imitator of other diseases, often diagnosed late or incorrectly as a condition with similar or overlapping clinical features[5,22].

In the presented case, the skin changes that initially stood out were the cutaneous lesions suspected of malignancy. Only after microscopic examination of the skin was it possible to confirm the diagnosis of lepromatous leprosy. However, skin changes typical of aging and photo exposure can be confounding factors, delaying the diagnosis of dermatoses, especially in a disease with a

wide variety of clinical forms[18]. In Brazil, 14,692 new cases were diagnosed in 2022, of which 1,449 cases presented a physical disability grade (PDG) of 2, reflecting high rates of late detection of the disease[1].

Several authors have described skin changes caused by leprosy in association with malignant skin neoplasms, not only with squamous cell carcinoma but also with basal cell carcinoma and melanoma[12,13,23,24]. In the context of squamous cell carcinomas associated with leprosy, the concurrence is common in scarred areas, especially older scars or regions of chronic ulcers[23,24].

The interaction between *M. leprae* infection and carcinogenesis is still not well established[13,14]. Although immune alterations are associated with the development of cutaneous carcinomas, it is suggested that the specificity of the immune response to *M. leprae* is not directly related to tumor onset[13,24,25].

Skin lesions, leprosy, and other dermatoses pose a diagnostic challenge for general practitioners and specialists[5,22,26]. In this context, epidemiological understanding is essential to establish the correct correlation between dermatological or histopathological changes, enabling early diagnosis even in the most challenging cases[27].

It is also noteworthy that males aged 60 years or older exhibit detection rates up to twice as high as those in the general population. Therefore, it is essential to conduct systematic examinations for these groups, starting at the primary care level, with professionals trained on the signs and symptoms of leprosy and active case finding through contact evaluation[28].

FINAL CONSIDERATIONS

The literature has previously described the coexistence of skin neoplasms with leprosy. However, the possible relationship between the natural history of these diseases has not yet been fully elucidated.

This report describes a case in which a cutaneous squamous cell carcinoma manifested concurrently with previously undiagnosed lepromatous leprosy in an elderly patient. Thus, this case may contribute to clinicians and pathologists by highlighting the need for attention to skin changes that can hinder the diagnosis of leprosy, especially in endemic regions, aiming to enable early diagnosis and reduce disease-related disabilities.

ETHICAL APPROVAL AND INFORMED CONSENT: *this study was previously submitted for approval by the Research Ethics Committee of the Federal University of Uberlândia, under CAAE: 42878620.0.0000.5152, in compliance with the National Health Council's regulations for research involving human subjects (Res. CNS 466/12).*

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