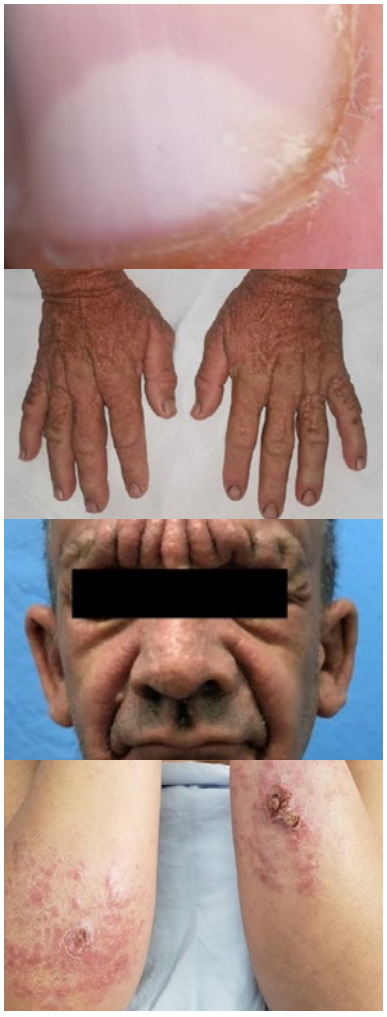
ISSN: 1989-8932

Medicina CUTÁNEA Ibero-Latino-Americana

ÓRGANO DE DIFUSION DEL COLEGIO IBERO-LATINO-AMERICANO DE DERMATOLOGÍA
www.MedicinaCutaneaILA.com

Volume 52, No. 1, January-April 2024



PERMANYER
www.permanyer.com

ISSN: 1989-8932

Medicina CUTÁNEA Ibero-Latino-Americana

ÓRGANO DE DIFUSION DEL COLEGIO IBERO-LATINO-AMERICANO DE DERMATOLOGÍA

www.MedicinaCutaneaILA.com

Volume 52
Issue 1
January-April 2024

Founders

Rubén David Azulay, Orlando Cañizares, Hernán Corrales Padilla, Francisco da Cruz Sobral, Luciano Domínguez Soto, José Gay Prieto, David Grinspan, Francisco Kerdel-Vegas, Antar Padilha Gonçalves, Joaquín Piñol Aguadé, Juan di Prisco, Augusto Salazar Leite

Editorial Board

Honorary Committee

Advisory Committee

Original papers should be deposited in their electronic version through the following URL:

https://publisher.mcila.permanyer.com/login.php

PERMANYER
www.permanyer.com

Permanyer
Mallorca, 310
08037 Barcelona (Cataluña), España
permanyer@permanyer.com

Permanyer México
Temístocles, 315
Col. Polanco, Del. Miguel Hidalgo
11560 Ciudad de México, México
mexico@permanyer.com

www.permanyer.com

ISSN: 0210-5187
eISSN: 1989-8932
Ref.: 10094AARG241

Medicina CUTÁNEA Ibero-Latino-Americana

PERMANYER

Check for updates

EDITORIAL

The World Congress of Dermatology Guadalajara 2027. A sample of what Ibero-Latin-America unity can achieve

El Congreso Mundial de Dermatología Guadalajara 2027. Una muestra de lo que la unidad iberolatinoamericana puede lograr

Jorge Ocampo-Candiani[1,2] and Mariel A. Isa-Pimentel[3]*

[1]Servicio de Dermatología, Hospital Universitario, Monterrey, México; [2]Facultad de Medicina, Universidad Autónoma de Nuevo León, Monterrey, México; [3]Servicio de Fototerapia, Instituto Dermatológico Dominicano y Cirugía de Piel Dr. Huberto Bogaert Díaz, Santo Domingo, República Dominicana

Dear colleagues,

Surely you have heard the exciting news, and if by any chance you have not yet, we are pleased to share with you that the next World Congress of Dermatology will be taking place in the beautiful city of Guadalajara, Mexico, from June 21st to June 26th, 2027. This achievement was the result of an international competition at the previous World Congress held in Singapore. In this competition, we faced Munich, representing Germany, Austria, and Switzerland. Our selection was endorsed by delegates representing over 190 societies from more than 95 countries worldwide. We deeply appreciate your trust and support, which drives us to take over this great responsibility with commitment and enthusiasm.

We are aware of the magnitude of the task this entails, as well as the extensive work it will require; however, this assignment not only motivates us to excel but also underscores an essential point: the choice of Mexico as the host is a shared achievement with the entire Ibero-Latin American community. We feel this accomplishment as a collective recognition and want to express our gratitude to all dermatological societies in Latin America, Spain, and Portugal, as well as to the Ibero-Latin American College of Dermatology, an institution that has forged a solid path in the global dermatological community.

We are taking a step toward the global arena, thanks to the hard work of those who came before us and the ongoing dedication and passion of those currently contributing with their ideas and innovations in the field of dermatology.

With this spirit, the Mexican Academy of Dermatology, the Mexican Society of Dermatology, the Mexican Society of Dermatological and Oncological Surgery, and the Mexican Society of Cosmetic and Laser Dermatology have all set themselves the ambitious goal of bringing the world's foremost dermatological congress to our territory. Mexico will become the face and spokesperson for all of us, motivating us to invite you to join us in this grand event, our event.

Considering the factors that define an exceptional destination for a congress of this magnitude, such as unbeatable weather, top-notch communications, world-class hotel and conference infrastructure, and above all, the warmth and hospitality of its people, Mexico emerges as the obvious choice. Our country stands out in multiple aspects; in the academic and professional field of dermatology, we have managed to excel internationally, presenting novel contributions and solutions

***Correspondence:**
Jorge Ocampo-Candiani
E-mail: jocampo2000@yahoo.com.mx

Date of reception: 06-12-2023
Date of acceptance: 08-02-2024
DOI: 10.24875/MCUTE.M24000001

Available online: 26-04-2024
Med Cutan Iber Lat Am. (Eng). 2024;52(1):1-2
www.MedicinaCutaneaILA.com

not only for common problems but also for those more complex and specific to our population, which we share with many of our Latin American colleagues. Together, we have made contributions that fill us with pride.

Mexico is a melting pot of traditions and modernity. Our cultural richness, resulting from the fusion of indigenous and primarily Spanish European heritage, has given rise to a unique and authentic culture. Despite aspiring to be at the forefront of knowledge and technology, we deeply value fundamental principles such as courtesy, kindness, friendship, and sincere treatment. This combination is the reason behind our growing popularity as a tourist and business destination. Those who visit us wish to return and those who get to know us hold a special affection for Mexico. This quality has endured despite the challenges we have faced, with the confidence to overcome them in the future. In Guadalajara, security is comparable to that of any city in the West world.

Organizing a congress of the magnitude and relevance of the World Congress of Dermatology demands a solid infrastructure and impeccable logistics. The City of Guadalajara is fully prepared for this challenge. It is one of the most beautiful cities in our country, boasting a hotel capacity of international quality, an efficient public transportation system, excellent air connections, and a convention center with adequate capacity to host an event of this magnitude.

In addition, Guadalajara offers invaluable attractions, such as the impressive murals of the Hospicio Cabañas, historically significant paintings, traditional markets, an amazing cathedral, excursions to the city of Tequila, the unique craftsmanship of Tonalá, its captivating historic center, and a variety of restaurants serving both local and international dishes. These elements will complement the experience of congress attendees and surely increase interest in participation.

Forty years ago, the International Congress of Dermatology (the previous name of the World Congress of Dermatology) was held, chaired by Dr. Antonio González Ochoa and with Dr. Luciano Domínguez Soto as the secretary-general, in Mexico City, an event that was a resounding success. Today, we have managed to have our city of Guadalajara selected as the venue and host of this congress. We extend a warm invitation for you to visit us in 2027, and we are confident that you will enjoy your stay. We are committed to balancing top-notch academic activities with a social program that reflects Mexican hospitality.

In Mexico, we consider kindness a duty and strive to ensure that our visitors feel at home. “Mi casa es tu casa” *(my home is your home)* is not just an empty phrase but a philosophy and a way of life that we hope you can experience. We eagerly look forward to welcoming you to Guadalajara in 2027.

Funding

The authors declare that this work was carried out with the authors’ own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Medicina CUTÁNEA Ibero-Latino-Americana

PERMANYER

Check for updates

ORIGINAL ARTICLE

Prevalence and demographic features of vitiligo in Colombia between 2015 and 2019

Prevalencia y características demográficas del vitiligo en Colombia entre los años 2015 y 2019

Melissa Rivera-Maldonado, Daniel G. Fernández-Ávila, Laura P. Charry-Anzola, and Felipe Omaña-Paipilla*

Departamento de Medicina Interna, Hospital Universitario San Ignacio, Bogotá, Colombia

Abstract

Background: *Vitiligo is a chronic autoimmune disease characterized by patches of depigmentation and/or poliosis, affecting more frequently the face, acral zones, and genitals. In consequence, it has a significant impact on the patient's life quality. There are some studies on vitiligo epidemiology in different countries; however, only one of them included the entire population.* **Objective:** *The objective of the study is to describe the prevalence and demographic characteristics of vitiligo in Colombia between 2015 and 2019.* **Materials and methods:** *A descriptive, cross-sectional study used the International Classification of Diseases (ICD-10) to classify cases of vitiligo, utilizing official data from the Colombian Ministry of Health.* **Results:** *A total of 70,702 cases of vitiligo were registered, indicating a global prevalence of 160 cases/100,000 inhabitants. Vitiligo was slightly more frequent in females compared to males (1.3:1 ratio). In children, the peak incidence occurred between 5 and 14 years old, while in adults, the majority of cases were observed in persons aged 51-60.* **Conclusions:** *This is the first descriptive study on the epidemiology of vitiligo in Colombia. The findings regarding female predominance and children's age of predominance are consistent with those in the medical literature, while the age of prevalence in adults and the global prevalence of vitiligo differ from previous reports.*

Keywords: *Colombia. Latin America. Vitiligo. Epidemiology.*

Resumen

Antecedentes: *El vitiligo es una enfermedad autoinmunitaria que se presenta con máculas acrómicas o poliosis, siendo más frecuentes en la cara, las zonas acrales y los genitales, por lo que genera un gran impacto en la calidad de vida de quienes lo padecen. Se han realizado estudios epidemiológicos del vitiligo en diferentes países, pero solo uno se realizó con la totalidad de la población.* **Objetivo:** *Describir la prevalencia y las características demográficas del vitiligo en Colombia entre los años 2015 y 2019.* **Material y métodos:** *Estudio descriptivo de corte transversal, en el que se utilizó la Clasificación Internacional de Enfermedades (CIE-10) para vitiligo, tomando datos del registro oficial del Ministerio de Salud de Colombia.* **Resultados:** *Se registraron 70,702 casos de vitiligo, con una prevalencia global de 160/100,000 habitantes. Hubo un ligero predominio femenino (relación mujer a hombre 1.3:1). Con respecto a la edad, en niños hubo un pico entre los 5 y 14 años, mientras que en adultos la mayoría de los casos se presentaron entre los 51 y 60 años.* **Conclusiones:** *Es el primer estudio que describe las características demográficas del vitiligo en Colombia. Los hallazgos de predominio femenino y la edad de mayor prevalencia en niños coinciden con lo reportado en la literatura, mientras que difieren en el pico de prevalencia en adultos y la prevalencia reportada en otros países.*

Palabras clave: *Colombia. América Latina. Vitiligo. Epidemiología.*

***Correspondence:**
Melissa Rivera-Maldonado
E-mail: melissa.rivera@javeriana.edu.co

Date of reception: 14-04-2023
Date of acceptance: 26-10-2023
DOI: 10.24875/MCUTE.M24000002

Available online: 26-04-2024
Med Cutan Iber Lat Am. (Eng). 2024;52(1):3-9
www.MedicinaCutaneaILA.com

Introduction

Vitiligo is an acquired disease in which there is selective damage to melanocytes, resulting in depigmentation of the skin and hair in the affected area, clinically presenting with asymptomatic achromic macules or poliosis, respectively[1,2]. Vitiligo can affect any body surface, but it often appears on the face, acral regions, or genitals, usually with symmetrical lesions[3]. Due to the anatomical areas involved, it often has a significant cosmetic impact and has even been associated with various psychiatric conditions[4]. Regarding its pathophysiology, there is a genetic basis, which, upon unclear environmental exposures, leads to oxidative stress and activation of the immune response, both innate and adaptive; the latter is characterized by antibodies against melanocytes as well as lymphocytes, mainly CD8+ T cells[2,5].

In terms of epidemiology, various studies have been conducted in the past 10 years in numerous countries, including Peru[6,7], Brazil[8-12], Germany[13], Japan[14], China[15,16], South Korea[17], Egypt[18], and the United States[19-21] (Table 1). These studies have found variable prevalence, ranging from 0.57% in Brazil to 0.91% in China and 1.68% in Japan. However, most of these studies were based on specific population groups or health-care centers. Only one study has comprehensive coverage of the entire population, conducted in South Korea using data from the national health security system of that country, finding a prevalence of 0.13%[17].

The objective of this study is to describe the prevalence and demographic characteristics of vitiligo in the Colombian population, based on data from the national registry of the Ministry of Health of Colombia.

Materials and methods

This is a descriptive, cross-sectional study using the integrated information system for social protection (SISPRO) of the Ministry of Health of Colombia. SISPRO is a tool designed to collect and provide standardized information about the health sector and service provision throughout the country. Specific health data are found in the Individual Records of Health Service Provision, which are constructed from the primary diagnosis code within the International Classification of Diseases 10th Revision of patient care in outpatient or hospital health services, which by law, physicians in the country are required to record. In addition, SISPRO receives information from various sources (population censuses, health surveys, and other administrative entities), which allows for verifying the accuracy of the data and even subjecting it to review by health entities in cases of inconsistencies.

Data were obtained from the entire country from January 1, 2015, to December 31, 2019. Consultations with individuals diagnosed with vitiligo (L80) were included. Information regarding population size, distribution by departments, sex, and age was obtained from the statistical projections of the National Administrative Department of Statistics (DANE). Subsequently, the prevalence was calculated for the total population and standardized by age, sex, and geographical location, with the total reported cases in SISPRO as the numerator and the respective demographic projections according to DANE information based on the projections of the last population census of 2018 as the denominator. Prevalence values are presented/100,000 inhabitants. Colombia has one of the highest health coverage rates in its health system, reaching 98.81%[22] according to the latest official measurement by the Ministry of Health in September 2022,[23] with a population of around 50 million inhabitants.

This project was approved by our hospital and university Ethics and Research Committee, with approval no. 18/2018 FM-CIE-0554-18.

Results

Between January 1, 2015, and December 31, 2019, 70,702 cases of vitiligo were identified, with a global prevalence of 160/100,000 inhabitants. There was a slight predominance of females, with a total of 40,646 cases (female-to-male ratio 1.3:1). Regarding age, there was an increase in cases between 5 and 14 years, followed by a decrease between 15 and 24 years and then a continuous rise in prevalence until reaching a peak between 55 and 59 years with a prevalence of 232 cases/100,000 inhabitants (Fig. 1). Regarding distribution by departments, the highest number of cases were recorded in Bogotá D.C. with a prevalence of 213 cases/100,000 inhabitants, followed by Antioquia and Atlántico with a prevalence of 188/100,000 inhabitants. In contrast, the department with the fewest registered cases was Vichada, with a prevalence of 16/100,000 inhabitants (Fig. 2).

Discussion

Vitiligo is an autoimmune and multifactorial disease with a significant impact on the patients' quality of life

Table 1. Epidemiological studies of vitiligo in the past 10 years in different countries

Authors	Year of publication	Country	Studied population	Study type	Prevalence	Gender with higher prevalence	Age of higher prevalence
Patel et al.[20]	2023	United States	Representative sample of children and adolescents with diagnosed or patient-reported vitiligo	Cross-sectional trial	Children: 0.84-1.52% Adolescents: 1.19-2.16%	NA	NA
Gandhi et al.[19]	2022	United States	Representative sample of adults aged 18-85 with diagnosed or patient-reported vitiligo	Cross-sectional trial	0.76-1.11%	Female	NA
Bibeau et al.[21]	2022	United States, Europe, Japan	Adults with diagnosed vitiligo suspected vitiligo, or signs of vitiligo	Cross-sectional trial	Total: 1.3% Europe: 1.6% United States: 1.4% Japan: 0.5%	Female	NA
Mohr et al.	2021	Germany	Two cohorts: 1) Workers from over 300 companies, aged 16-70, assessed between 2004 and 2014 2) Patients with vitiligo from the mandatory insurance system in 2010	Cross-sectional trial	Workers' cohort: 0.77% Insurance cohort: 0.17%	Workers cohort: men. Insured cohort: women	Workers cohort: 40-49 years Insurance cohort: 60-70 years
Tang et al.[15]	2021	China	Cluster samples of adults in the Beixinjing community, Shanghai, between October 2009 and January 2010	Secondary analysis of cross-sectional trial	0.91%	Male	71-80 years
Martins et al.[11]	2020	Brazil	Patients younger than 18 diagnosed with vitiligo, whose age at disease onset was < 13, evaluated at Professor Rubem David Azulay Dermatology Clinic from 2006 through 2014	Cross-sectional trial	NA	Female	NA
Silveira Tolentino et al.[9]	2019	Brazil	60 413 individuals surveyed for autoimmune diseases in 26 primary care centers in the Aguas For mosas micro region between January and December 2016	Cross-sectional trial	0.13%	Female	NA

(Continues)

Table 1. Epidemiological studies of vitiligo in the past 10 years in different countries (*continued*)

Authors	Year of publication	Country	Studied population	Study type	Prevalence	Gender with higher prevalence	Age of higher prevalence
Silva and Miot[8]	2018	Brazil	Random sample of individuals from 87 Brazilian municipalities with over 300,000 inhabitants, representing approximately 40% of the Brazilian population, between January and June of 2017	Cross-sectional study	0.005700	Female	NA
Lee et al.[17]	2015	South Korea	Patients diagnosed with vitiligo enrolled in the Social Security Review and Evaluation Service between 2009 and 2011	Cross-sectional study	0.13%	Female	Bimodal distribution: 5-15 years and 45-55 years
De Barros et al.[12]	2014	Brazil	Patients diagnosed with vitiligo at the Dermatology Clinic, ABC Medical School, evaluated between January 2001 and May 2006	Cross-sectional trial	NA	Female	10-20 years
Wang et al.[16]	2013	China	Cluster sampling of residents from six cities in China	Cross-sectional trial	0.56%	Male	> 70 years
Yamamah et al.[18]	2012	Egypt	2194 children under 18 years old in South Sinai between August 2008 and August 2009	Cross-sectional trial	0.18%	NA	NA
Furue et al.[14]	2011	Japan	Hospitalized and outpatient patients seen at 170 health centers in May, August, and November 2007, and February 2008	Cross-sectional trial	1.68%	NA	60-70 years
Nunes and Esser[10]	2011	Brazil	Patients seen at the outpatient dermatology centers AME Unisul and HU UFSC between November 2003 and October 2009	Cross-sectional trial	NA	Female	NA
Rodríguez and Chávez[7]	2007	Peru	Pediatric patients seen in the outpatient pediatric dermatology clinic at the EsSalud Chiclayo National Hospital between July 2003 and July 2006	Cross-sectional trial	5.5%	Female	School age

(Continues)

Table 1. Epidemiological studies of vitiligo in the past 10 years in different countries (*continued*)

Authors	Year of publication	Country	Studied population	Study type	Prevalence	Gender with higher prevalence	Age of higher prevalence
Valverde and Grados	2007	Peru	Patients clinically diagnosed with vitiligo treated at the outpatient dermatology clinic of the Regional Teaching Hospital of Trujillo between January 1, 1994, and December 31, 2003	Cross-sectional trial	1.5% of diagnoses treated at the hospital	Female	NA

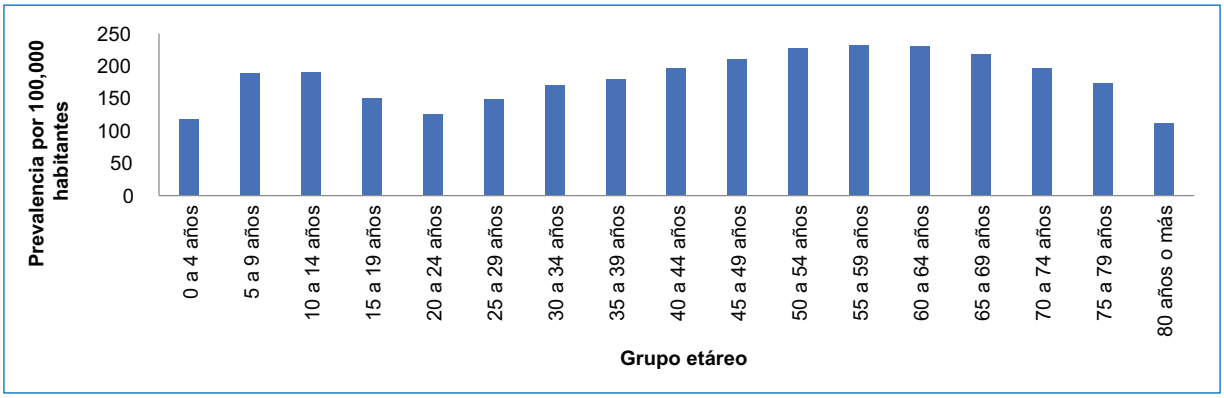


Figure 1. Prevalence of vitiligo by age group from 2015 to 2019.

due to its association with psychiatric disorders such as depression and anxiety as well as feelings of stigmatization and avoidant behaviors[4]. In addition, it has been associated with other autoimmune diseases, with the most common being Hashimoto's thyroiditis[24], diabetes mellitus, and alopecia areata[2]. According to the results of our study, vitiligo has a prevalence of 160 cases/100,000 inhabitants, with a slight predominance in females. Although the peak prevalence occurred between 55 and 59 years, it was evident that most cases among the pediatric population occurred between the ages of 5 and 14 years.

In Latin America, several retrospective and cross-sectional studies have been conducted on the epidemiology of vitiligo. In Peru, Valverde and Grados[8] established that vitiligo accounted for 1.5% of all adult patients seen in outpatient consultations over a 9-year period. In Brazil, De Barros et al.[12] and Nunes and Esser[10] also characterized patients diagnosed with vitiligo seen in outpatient consultations. In addition, Silva and Miot[8] conducted telephone calls to residents of 87 municipalities in the country with a total of 17,000 inhabitants, finding a prevalence of 0.57%, which was higher than the one found in our population. Silveira Tolentino et al.[9] aimed to establish the prevalence of 24 autoimmune diseases, including vitiligo, in 26 health centers from Brazil and found it to be the second most common autoimmune disease, with 132.4 cases/100 000 inhabitants, slightly lower compared to our prevalence of 160/100 000 inhabitants.

In the United States, a study conducted through surveys on a representative sample of the adult population diagnosed with vitiligo or reported by participants found a prevalence of 0.76 up to 1.11%[19]. In addition, the study considered patients without a vitiligo diagnosis, suggesting that up to 40% of adults with vitiligo in the United States are undiagnosed. Bibeau et al.[21] also conducted another survey-based study, finding a prevalence of 1.4% of vitiligo in adults in the United States, which falls within the range of the previously mentioned study and is almost eight times higher than the prevalence in our population. This same study also evaluated the

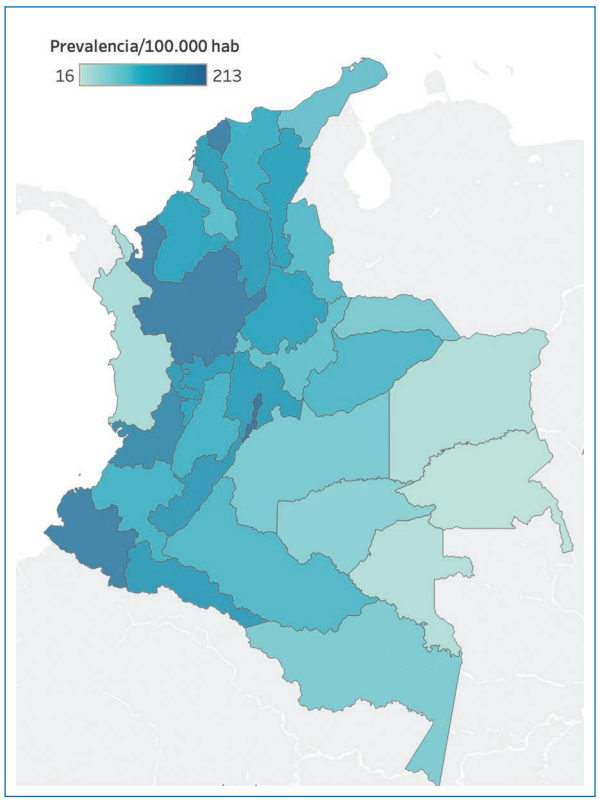


Figure 2. Geographic distribution of vitiligo cases in the 2015-2019 period by departments in the Colombian population.

prevalence of vitiligo in adults in Europe and Japan, finding the highest prevalence in Europe, at 1.6%. This result is higher compared to a study in Germany conducted in two cohorts: the first conducted a dermoscopy of workers from over 300 companies, while the second study conducted a dermoscopy on individuals with vitiligo covered by a health company that covers nearly 90% of the country[13]. The first cohort had a prevalence of vitiligo of 0.77%, more common in men, while the second cohort had a prevalence of 0.17%, more common in women, with these latter results being more similar to those of our population. The similarities found between our study and the second cohort and the differences found with the first cohort could be explained by the sampling methods used in each of the study groups since the second cohort achieved greater population coverage.

Japan had the lowest prevalence found by Bibeau et al.[21], at 0.5%. However, a previous multicenter cross-sectional study conducted with 170 health centers, with information from hospitalized and outpatient patients, found a higher prevalence of 1.68%, with a higher frequency between the seventh and eighth decades of life[14].

In South Korea, a study with similar characteristics to ours was conducted based on the database review of the Health Insurance Review and Assessment Service (HIRA) of patients diagnosed with vitiligo between 2009 and 2011. We should mention that in that country, all citizens are required to join HIRA. In this study, the prevalence found was 0.13%[17], which is very similar to that of our study. In addition, the age distribution is similar, and they obtained the same female-to-male ratio, making the results more similar to those found in our study.

Although most studies describe a female predominance, we have two studies in China reporting the opposite. The first was conducted in a community in Shanghai with patients older than 18 years, with a prevalence of 0.91%[15]. The second was a multicenter cluster sampling study conducted in six cities from different regions, where a prevalence of 0.56% was found in a sample of 17,345 individuals[16].

Regarding the pediatric population, there is a study from Peru[7] and one from Brazil[11] of patients seen in outpatient consultations. Both studies reported a female predominance. Regarding age, a mean age of 8.8 years was reported in children from Peru, while an age of onset of vitiligo of 5.9 years was reported in Brazil. In Egypt, a cross-sectional study was also conducted to determine the prevalence of dermatological diseases in individuals younger than 18 years, finding a vitiligo prevalence of 0.18%[18]. In the United States, in a representative sample of children and adolescents, a vitiligo prevalence of 0.84% up to 1.52% in children and 1.19% up to 2.16% was found among adolescents. Furthermore, the results suggest that up to 50% of children and adolescents in that country do not have a clinical diagnosis of vitiligo[20].

The reported worldwide prevalence of vitiligo ranges from 0.5% up to 2%[25]; however, the prevalences of some of the aforementioned studies, including our own, are below this range, showing significant variation not only in prevalence but also in distribution by sex and age, which could be influenced by various factors such as the phototype of the subjects, access to health care services, frequency of consultations, and even life expectancy in each country. Our results were very similar to those found in South Korea, where a study with a methodology similar to ours and nearly complete population coverage was conducted, suggesting that the type of study, as well as population coverage, play a role in the epidemiology of vitiligo, highlighting the need for more epidemiological studies with greater population coverage to achieve greater certainty regarding the epidemiology of vitiligo.

Among the limitations of our study, we should mention that, due to the nature of the SISPRO registry, it is not possible to establish the incidence or age of onset nor delve into disease-specific data such as its duration, anatomical sites involved, or patients' phototypes. In addition, prevalence is conditioned by the number of consultations, which could mean underreporting of cases where vitiligo is not the primary diagnosis or cases where patients do not seek medical attention. Furthermore, we could not establish whether the diagnosis was made by a dermatologist or by a general practitioner or specialist from another field. Although vitiligo is associated with other autoimmune diseases, the methodology used in this study did not allow us to establish these associations.

Conclusions

Our study is the first to assess the prevalence of vitiligo in Colombia within the context of a health-care system with nearly universal coverage, and it represents an effort toward building a better understanding of the epidemiology of vitiligo worldwide. In addition, it allows for the establishment of strategies for more timely diagnosis in our country, as well as education for both patients and other specialists, beyond dermatologists, regarding the clinical aspects of the disease and its association with autoimmune and psychiatric conditions. Furthermore, it opens up the possibility for new studies in which not only the epidemiology of vitiligo is evaluated but also its prevalence in relation to the diversity of phototypes presents in our country, as well as opportunities for care.

Funding

The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines, depending on the type and nature of the study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Nicolaidou E, Mastraftsi S, Tzanetakou V, Rigopoulos D. Childhood vitiligo. Am J Clin Dermatol. 2019;20:515-26.
2. Bergqvist C, Ezzedine K. Vitiligo: a review. Dermatology. 2020;236:571-92.
3. Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, et al., editores. Fitzpatrick's Dermatology. 9th ed. New York, NY: McGraw-Hill; 2019.
4. Ezzedine K, Eleftheriadou V, Jones H, Bibeau K, Kuo F, Sturm D, et al. Psychosocial effects of vitiligo: a systematic literature review. Am J Clin Dermatol. 2021;22:757-74.
5. Ongenae K, Geel N Van, Naeyaert J-M. Evidence for an autoimmune pathogenesis of vitiligo. Pigment Cell Res. 2003;16:90-100.
6. Valverde J, Grados MA. Vitíligo: aspectos clínicos y epidemiológicos. Folia Dermatol Peru. 2007;18:18-22.
7. Rodríguez-Barboza R, Chávez-Esquives J. Vitíligo en niños: estudio epidemiológico. Dermatol Peru. 2007;17:24-9.
8. Silva CC, Miot HA. Prevalence of vitiligo in Brazil — a population survey. Pigment Cell Melanoma Res. 2018;31:448-50.
9. Silveira Tolentino Jr D, Meireles de Oliveira C, Miranda de Assis E. Population-based study of 24 autoimmune diseases carried out in a Brazilian microregion. J Epidemiol Glob Health. 2019;9:243-51.
10. Nunes DH, Esser LMH. Perfil epidemiológico dos pacientes com vitiligo e sua associação com doenças da tireoide. An Bras Dermatol. 2011;86:241-8.
11. Martins CP dos S, Hertz A, Luzio P, Paludo P, Azulay-Abulafia L. Clinical and epidemiological characteristics of childhood vitiligo: a study of 701 patients from Brazil. Int J Dermatol. 2020;59:236-44.
12. De Barros JC, Machado Filho CD, Abreu LC, de Barros JA, Paschoal FM, Nomura MT, et al. A study of clinical profiles of vitiligo in different ages: an analysis of 669 outpatients. Int J Dermatol. 2014;53:842-8.
13. Mohr N, Petersen J, Kirsten N, Augustin M. Epidemiology of vitiligo — a dual population-based approach. Clin Epidemiol. 2021;13:373-82.
14. Furue M, Yamazaki S, Jimbow K, Tsuchida T, Amagai M, Tanaka T, et al. Prevalence of dermatological disorders in Japan: a nationwide, cross-sectional, seasonal, multicenter, hospital-based study. J Dermatol. 2011;38:310-20.
15. Tang L, Li F, Xu F, Yan S, Zhou J, Li J, et al. Prevalence of vitiligo and associated comorbidities in adults in Shanghai, China: a community-based, cross-sectional survey. Ann Palliat Med. 2021;10:8103-11.
16. Wang X, Du J, Wang T, Zhou C, Shen Y, Ding X, et al. Prevalence and clinical profile of vitiligo in China: a community-based study in six cities. Acta Derm Venereol. 2013;93:62-5.
17. Lee H, Lee M-H, Youn Lee D, Young Kang H, Ho Kim K, Seong Choi G, et al. Prevalence of vitiligo and associated comorbidities in Korea. Yonsei Med J. 2015;56:719-25.
18. Yamamah GA, Emam HM, Abdelhamid MF, Elsaie ML, Shehata H, Farid T, et al. Epidemiologic study of dermatologic disorders among children in South Sinai, Egypt. Int J Dermatol. 2012;51:1180-5.
19. Gandhi K, Ezzedine K, Anastassopoulos KP, Patel R, Sikirica V, Daniel SR, et al. Prevalence of vitiligo among adults in the United States. JAMA Dermatol. 2022;158:43-50.
20. Patel R, Pandya AG, Sikirica V, Gandhi K, Daniel SR, Anastassopoulos KP, et al. Prevalence of vitiligo among children and adolescents in the United States. Dermatology. 2023;239:227-34.
21. Bibeau K, Pandya AG, Ezzedine K, Jones H, Gao J, Lindley A, et al. Vitiligo prevalence and quality of life among adults in Europe, Japan and the USA. J Eur Acad Dermatol Venereol. 2022;36:1831-44.
22. Fernández-Ávila DG, Bernal-Macías S, Rincón-Riaño DN, Gutiérrez Dávila JM, Rosselli D. Prevalence of systemic lupus erythematosus in Colombia: data from the national health registry 2012-2016. Lupus. 2019;28:1273-8.
23. Ministerio de Salud de Colombia. Cifras de aseguramiento en salud. 2021. Disponible en: https://www.minsalud.gov.co/proteccionsocial/Paginas/cifras-aseguramiento-salud.aspx
24. Kakourou T, Kanaka-Gantenbein C, Papadopoulou A, Kaloumenou E, Chrousos GP. Increased prevalence of chronic autoimmune (Hashimoto's) thyroiditis in children and adolescents with vitiligo. J Am Acad Dermatol. 2005;53:220-3.
25. Zhang Y, Cai Y, Shi M, Jiang S, Cui S, Wu Y, et al. The prevalence of vitiligo: a meta-analysis. PLoS One. 2016;11:e0163806.

Medicina CUTÁNEA Ibero-Latino-Americana

PERMANYER

Check for updates

ORIGINAL ARTICLE

Aesthetic and functional results of Mohs micrographic surgery in non-melanoma skin cancer

Resultados estéticos y funcionales de la cirugía micrográfica de Mohs en cáncer de piel no melanoma

Edgar M. Olmos-Pérez[1], Danney Gómez-Angulo[1], Paola Rojas-Angarita[1], Laura V. Vargas-Gualdron[1], Santiago A. Ariza-Gómez[1], and Carlos A. Castro-Moreno[2]*

[1]Departamento de Dermatología; [2]Departamento de Epidemiología. Fundación Universitaria de Ciencias de la Salud, Hospital de San José de Bogotá, Bogotá, Colombia

Abstract

Background: *Non-melanoma skin cancer is the most common human neoplasm. Mohs micrographic surgery (MMS) is the standard of care for high-risk subtypes, allowing tumor removal with the best oncological, esthetic, and functional results. The purpose of this study is to describe the esthetic and functional results of MMS in patients with a diagnosis of basal cell carcinoma and squamous cell carcinoma.* **Material and methods:** *Ambispective cohort study was performed in three dermatological centers in Bogota, Colombia, with patients that have been operated on with MMS between 2012 and 2019. The study subjects answered through a telephonic interview the skin cancer module of the FACE-Q satisfaction scale questionnaire in the period between June and August 2019.* **Results:** *530 patients with 650 tumors were included. 494 patients completed the skin cancer module of the FACE-Q scale. 92% of patients presented adequate healing in the first follow-up year and, at the same time, a low percentage of alterations regarding functional results. The FACE-Q questionnaire was conducted with a median of 40 months after the surgery, with an average satisfaction of 93.2%.* **Conclusions:** *The MMS generates excellent functional and esthetic results in patients with NMSC, as demonstrated by the high satisfaction evidenced in the FACE-Q scale by patients.*

Keywords: *Mohs surgery. Basal cell carcinoma. Squamous cell carcinoma. Esthetic satisfaction. Functional results. FACE-Q.*

Resumen

Antecedentes: *El cáncer de piel no melanoma (CPNM) es la neoplasia más frecuente del ser humano. La cirugía micrográfica de Mohs (CMM) es el tratamiento de elección para el CPNM de alto riesgo, permitiendo la eliminación del tumor con mejores resultados oncológicos, estéticos y funcionales.* **Objetivo:** *Describir los resultados estéticos y funcionales de la CMM en pacientes con diagnóstico de carcinoma basocelular y carcinoma escamocelular, utilizando la escala de satisfacción FACE-Q.* **Material y métodos:** *Estudio de cohorte ambispectiva realizado en tres centros dermatológicos de Bogotá, Colombia, en pacientes que fueron manejados con CMM desde 2012 hasta 2019. Los pacientes completaron el módulo de cáncer de piel de la escala de satisfacción FACE-Q desde junio hasta agosto de 2021 mediante contacto telefónico.* **Resultados:** *Se incluyeron 530 pacientes con 650 tumores. El 93.2% de los pacientes completaron la escala FACE-Q. El 92% presentaron adecuada cicatrización en el primer año de seguimiento, con bajos porcentajes de alteraciones en los resultados funcionales. La encuesta FACE-Q se realizó una mediana de 40 meses posterior a la cirugía, con una satisfacción*

***Correspondence:**
Laura V. Vargas-Gualdron
E-mail: lvgualdro@fucsalud.edu.co

Date of reception: 05-05-2023
Date of acceptance: 26-10-2023
DOI: 10.24875/MCUTE.M24000003

Available online: 26-04-2024
Med Cutan Iber Lat Am. (Eng). 2024;52(1):10-15
www.MedicinaCutaneaILA.com

media del 93.2%. **Conclusiones:** *La CMM genera excelentes resultados funcionales y estéticos en los pacientes con CPNM, demostrado por los altos índices de satisfacción evidenciados en la escala FACE-Q por los pacientes.*

Palabras clave: *Cirugía de Mohs. Carcinoma basocelular. Carcinoma escamocelular. Satisfacción estética. Resultados funcionales. FACE-Q.*

Introduction

Non-melanoma skin cancer (NMSC) is the most common neoplasm in humans, with an incidence that continues to rise worldwide[1]. It frequently affects the face and neck, which is crucial as functional and esthetic outcomes are significant considerations when determining the type of management and reconstruction to be undertaken due to the psychosocial impact it has on the patient[2,3]. Therefore, Mohs micrographic surgery (MMS) should be considered as the primary treatment option for potentially curable NMSC with a high risk of recurrence and in areas where tissue preservation is necessary to achieve adequate functional and esthetic results[4-6].

In a study conducted by Lee et al., variables associated with esthetic outcomes following skin cancer surgery were identified, providing a framework for the development of an instrument to collect patient-reported outcomes: the FACE-Q scale[7]. This instrument thoroughly quantifies the impact of facial skin cancer on final outcomes, from healing to adverse events associated with treatment and the entire health-care process[7].

Subsequently, we conducted an ambispective cohort study on esthetic and functional outcomes following the resection of NMSC through MMS, also evaluated using the FACE-Q scale, in three dermatological centers in the city of Bogotá, Colombia.

Methods

We conducted an ambispective cohort study, which was approved by the Universidad de Ciencias de la Salud Foundation ethics and research committee with respective consents, including all patients treated with MMS with a confirmed diagnosis of basal cell carcinoma or squamous cell carcinoma in three dermatological centers in Bogotá from 2012 through 2019.

Esthetic and functional outcomes recorded in health records during at least one of the two follow-ups (the first within the first 6 months and the second between 6 and 12 months later) were evaluated as outcomes. Patients who were reconstructed by specialties other than dermatology (due to difficulty in follow-up) or with a past medical history of radiotherapy as adjuvant treatment (due to changes in the quality of the surrounding skin) were excluded.

Subsequently, all researchers conducted surveys (appearance, quality of life, adverse events, and patient experience) from the skin cancer module of the FACE-Q. Each scale consists of 8-10 questions, scoring from 0 to 100, with higher values indicating greater satisfaction with facial appearance. Before the implementation of the scale, the corresponding license was obtained from its authors, and it was applied in the official Spanish translation format. The FACE-Q skin cancer module was conducted through telephone call by the researchers, once per patient (not per number of tumors).

Data collection was conducted ambispectively; patient background and surgical procedure-related variables were taken from the health records retrospectively, while the FACE-Q score and survival variables were obtained through phone call.

Procedure

As relevant data from the health records for the analysis, sociodemographic variables, skin type, course of the disease, cancer type (basal cell carcinoma or squamous cell carcinoma), tumor type (primary, recurrent, or persistent), previous treatment (conventional surgery, imiquimod, or other [cryosurgery, 5-fluorouracil, electrodesiccation-curettage]), localization by anatomical sites to provide a more specific description of esthetic and functional outcomes (nose, orbital region, lip region, ear region, malar region, frontotemporal region, scalp), clinical tumor size, surgical states, timing of care (time elapsed between the decision for MMS [delivery of the medical order in the office] and when it was actually performed), tumor invasion (subcutaneous tissue, muscle, cartilage, bone), reconstruction technique (direct closure, flap, graft, second intention closure, combined techniques), and esthetic and functional outcomes were recorded. Specific and overall survival outcomes were explored prospectively.

Telephone follow-up was conducted to apply the scar appearance satisfaction scale from the skin cancer module of the FACE-Q scale to measure patient perceptions of esthetic outcomes.

Analysis

Sociodemographic, clinical, surgical, esthetic, and functional results were presented as measures of central tendency and dispersion if they were quantitative variables, based on data distribution. Qualitative variables were expressed as absolute and relative frequencies.

Patient satisfaction was expressed as an average with standard deviations (SD), and to compare the score of the skin cancer module of the FACE-Q scale, the mean FACE-Q score was calculated with each variable of interest (sex, age, skin type, cancer type, location, and reconstruction technique). Patient age was categorized into 2 groups: < 65 and ≥ 65 years.

To determine differences in the FACE-Q score average among the different variables of interest, the Student's t-test was used for dichotomous variables and the ANOVA one for variables with > 2 categories.

Survival analysis after the surgical procedure was performed using Kaplan–Meier analysis, defining the patient's status as reported through telephone call as the outcome. The database was created in Excel and analyzed using Stata 13 software.

Results

A total of 1074 patients with 1286 tumors meeting the inclusion criteria were included. After applying the exclusion criteria, 530 patients with 650 tumors were included who received a telephone call, and it was found that 36 had died. Therefore, the FACE-Q survey from the skin cancer module was applied to the 494 surviving patients. Of these, 294 (59.5%) were followed up during the first 6 months and 149 (30.1%) for up to 1 year.

Sociodemographic results

The median age was 68 years (interquartile range [IQR]: 57-77), and women represented 58.5% (n = 310) (Table 1).

Clinical results

A total of 92.9% (n = 604) of carcinomas were basal cell carcinomas, with the nodular subtype accounting for 67.5% (n = 434), followed by trabecular at 35.6% (n = 229), micronodular at 24.5% (n = 222), superficial at 6% (n = 39), and morpheaform subtype at 0.9% (n = 6). On the other hand, 7% (n = 46) were squamous cell carcinomas, with the well-demarcated subtype being the most prevalent at 41.3% (n = 19).

Table 1. Sociodemographic, clinical, and surgical characteristics of the patients

Variable	n	%
Sex (n = 530)		
Female	310	58.5
Male	220	41.5
Fitzpatrick phototype (n = 241)		
II	36	14.9
III	148	61.4
IV	57	23.6
Cancer type (n = 650)		
Basal cell	604	93
Squamous cell	46	7.0
Tumor relapse (n = 650)		
Primary	597	91.8
Recurrent	47	7.2
Persistent	6	0.9
Previous treatment (n = 53)		
Conventional surgery	41	77.3
Imiquimod	2	3.2
Other	10	18.8
Location (n = 650)		
Nasal region	260	40
Orbital region	116	17.8
Lip region	43	6.6
Ear region	54	8.3
Malar region	118	18.1
Frontotemporal region	44	6.7
Scalp	15	2.3
Tumor invasion		
Reticular dermis	342	52.6
Subcutaneous tissue	98	15
Muscle	189	29
Perichondrium	18	2.7
Periosteum	3	0.4
Reconstruction technique (n = 650)		
Direct closure	74	11.3
Flap	469	72.1
Graft	90	13.8
Graft + Flap	13	2.0
Secondary intention closure	4	0.6

Data on MMS stages were obtained for 97.6% (n = 635) of tumors. We should mention that 52.1% of tumors were completely excised in one stage (n = 331), 40.6% in 2 stages (n = 258), 6.7% in 3 stages (n = 43), 0.31% in 4 stages (n = 2), and 0.16% in 5 stages for complete excision (n = 1).

Esthetic results

Among the 584 tumors evaluated within the first month, 0.8% (n = 5) presented acute complications post-MMS, corresponding to suture dehiscence. Within

the first 6 months, 89% of patients (n = 326) presented eutrophic scars, 9.2% (n = 34) were hypertrophic, and 1.6% (n = 6) were atrophic (Fig. 1).

Functional results

Within the first 6 months of follow-up, ectropion was found in 2% (n = 6) of operated tumors and 0.3% (n = 1) had lagophthalmos, while at 1 year, 2.6% (n = 4) presented ectropion and 0.6% (n = 1) had lagophthalmos.

In the ear region, it was observed that 1% (n = 3) had ear retraction, and in 0.3% (n = 1), helix preservation was not achieved, while at 1 year, it was observed that 0.6% (n = 1) exhibited ear retraction.

In the lip region, 0.3% (n = 1) of the tumors did not allow lip sealing, and in 0.3% (n = 1), suction was impaired, while at 1 year, 0.6% (n = 1) did not allow lip sealing.

In the nasal region, 1% (n = 3) of tumors caused nasal alar retraction, while at 12 months, 1.3% (n = 2) did so.

Patient satisfaction

The scar appearance survey from the skin cancer module of FACE-Q was conducted with a median of 40 months after surgery (IQR, 29-52 months).

Overall, the cohort was highly satisfied with their medical care. The mean score in the scar appearance domain of the skin cancer module of the FACE-Q survey was 93.2% (SD, 11.9) (Table 2).

No patients with recurrences after MMS were evidenced within the evaluated data.

Mortality

The all-cause mortality rate was 6.8% (n = 36) (Fig. 2). Of the deceased patients, 19.4% were due to COVID-19, all of whom were men with a median age of 70 years. A total of 5.6% of patients died due to squamous cell carcinoma metastasis (n = 2) and the remaining 75% (n = 27) from other causes. No data on other types of NMSC-causing mortality were obtained in this study.

Discussion

MMS has become the standard of care for the management of high-risk NMSC[8]. Therefore, we present an ambispective cohort that allowed us to evaluate the esthetic and functional outcomes of MMS in NMSC, using the FACE-Q satisfaction scale as an evaluator of quality of life and healing.

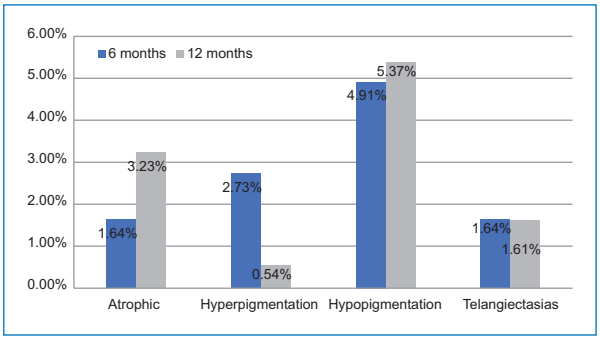


Figure 1. Esthetic outcomes at the 6- and 12-month follow-up.

The mean age of the study population was 68 years, with a higher number of women, which is consistent with other studies, such as the one conducted at the University Hospital of Basel, Switzerland, where the age range was 54-84 years, with a mean of 63 years, and a higher percentage of female population[9].

In the evaluated patients, the most frequent location of NMSC was nasal, which is consistent with the study conducted by Carvalho et al. in São Paulo, where 101 patients with basal cell carcinoma were evaluated, and the most frequent location was the nasal region, followed by the periorbital region. In addition, they also exhibited more esthetic or functional complications[10].

The application of the FACE-Q scale allowed us to evaluate 93.2% of the patients included in the study, with a mean global satisfaction score of 93.2%, which demonstrates a high degree of satisfaction after MMS. This is also demonstrated in other studies, such as in the cohort of Asgari et al., where patients with NMSC treated with MMS had predictors of higher satisfaction, better skin quality, and better health status[6].

Among the patients evaluated with the FACE-Q scale, 59.5% underwent the first follow-up at 3-6 months, while 30.1% were follow-up at 6 and 12 months, demonstrating that the possibility of follow-up and control by the same center or specialist is a difficult task.

This was also evidenced by the study conducted at the University of Chicago and Memorial Sloan Kettering Cancer Center, where it was found that the recruitment and follow-up of skin cancer patients are highly variable and impacted by multiple factors, depending on the possibility of contact with the patient or the interest in participating in the study[11].

Regarding functional results, the most frequent change was ectropion, in 2%, while the least common changes were ear retraction, lip seal changes, and nasal alar

Table 2. Comparison of scores from the skin cancer module of the FACE-Q scale by demographic and clinical variables.

Variable	Code	n	Mean (SD)	p
Gender*	Female Male	296 198	92.01 (13.44) 94.99 (8.93)	0.0063
Age*	< 65 years ≥ 65 years	181 310	93.50 (11.49) 92.97 (12.21)	0.6381
Fitzpatrick phototype*	2 3 4	33 140 53	93.58 (15.02) 90.72 (12.57) 92.51 (11.55)	0.8700
Cancer type†	Basal cell Squamous cell	565 39	93.08 (11.93) 93.31 (11.48)	0.9086
Location†	Nose Orbital region Lip region Ear region Malar region Frontotemporal region Scalp	246 112 40 47 109 37 13	91.90 (12.73) 93.13 (12.05) 90.13 (12.92) 94.49 (11.00) 95.51 (10.67) 95.05 (8.84) 93.69 (7.47)	0.0825
Reconstruction technique†	Direct closure Flap Graft Flap + Graft Secondary intention closure	72 433 83 12 4	96.46 (6.11) 92.80 (12.22) 91.59 (13.88) 91.67 (9.96) 100 (0.0)	0.0637

SD: standard deviation.
*n = 530 patients.
†n = 650 tumors.

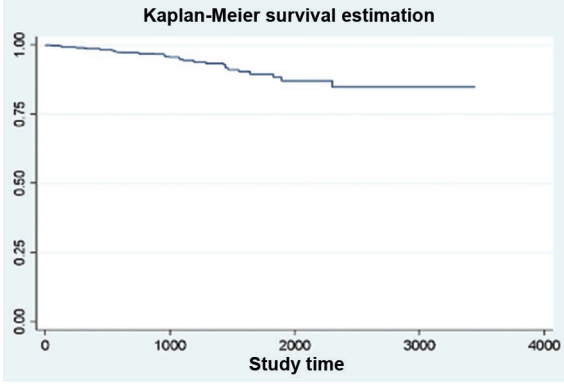


Figure 2. Survival graph (considering all-cause mortality, in days).

retraction. Factors associated with a higher risk of functional changes were advanced age and high-risk histological patterns (trabecular). This correlates with functional changes, as evidenced in an analysis conducted at the University of Rochester with 320 patients, where ectropion and retractions, or nasal stenosis, were the main findings[12].

We should mention that our study has a considerable sample size, with a high response and satisfaction rate in the FACE-Q survey. This is consistent with what Vaidya et al.[11], reported who conducted a cross-sectional study and applied the satisfaction scale to 408 patients, with a response rate of 39%. In addition, in our study, in-person follow-up was conducted for up to 1 year and remote follow-up for up to 9 years, confirming that healing improves over time, which allows for a reference on the possible progression of patients in relation to their esthetic and functional outcomes.

Similarly, our study confirms that MMS achieves high functional outcomes in addition to the known oncological results, allowing for the preservation of patient quality of life. This was also evidenced in a prospective study conducted at the University of Nebraska, where 226 patients who underwent MMS for NMSC showed a high satisfaction rate, with a significant percentage being satisfied with the procedure and its results[9].

Limitations

We consider that the limitations of this study are based on the difficulty in complying with all established follow-ups and the retrospective collection of data. In addition, subgroups of patients with lower scores on the FACE-Q scale were too small to perform statistical analyses of

associations, and the surveys were conducted remotely by medical personnel to facilitate their application due to the size of the population; however, it is designed to be self-administered, which could lead to a conformity bias. Therapies performed for the described complications were not evaluated in this study, and we consider this to be an interesting new line of research. Nevertheless, the study has a significant number of patients in whom esthetic and functional outcomes are evaluated, with long follow-up periods, which provides valuable information to the medical community and facilitates decision-making when intervening in patients with NMSC.

Conclusions

MMS generates excellent functional and esthetic outcomes in patients with NMSC, which can be demonstrated by the high satisfaction rates evidenced in the scales of the skin cancer module of the FACE-Q conducted by patients. This ultimately allows for the preservation of patient quality of life, also leading to better functional outcomes.

Funding

The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for the analysis and publication of routinely acquired clinical data, and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Pozzobon FC, Acosta AE, Castillo JS. Cáncer de piel en Colombia: cifras del Instituto Nacional de Cancerología. Rev Asoc Colomb Dermatol. 2018;26:12-17.
2. Burdon-Jones D, Thomas P, Baker R. Quality of life issues in nonmetastatic skin cancer. Br J Dermatol. 2010;162:147-51.
3. Hoogewerf CJ, van Baar ME, Middelkoop E, van Loey NE. Patient reported facial scar assessment: directions for the professional. Burns. 2014; 40:347-53.
4. Ariza S, Espinosa S, Naranjo M. Nonsurgical therapies for basal cell carcinoma: a review. Actas Dermosifiliogr. 2017;108:809-17.
5. Bath-Hextall FJ, Perkins W, Bong J, Williams HC. Interventions for basal cell carcinoma of the skin. Cochrane Database Syst Rev. 2007; (1):CD003412.
6. Asgari MM, Bertenthal D, Sen S, Sahay A, Chren MM. Patient satisfaction after treatment of nonmelanoma skin cancer. Dermatol Surg. 2009; 35:1041-9.
7. Lee EH, Klassen AF, Lawson JL, Cano SJ, Scott AM, Pusic AL. Patient experiences and outcomes following facial skin cancer surgery: A qualitative study. Australas J Dermatol. 2016;57(3):e100-4. DOI: 10.1111/ajd.12323.
8. Dokic Y, Nguyen QL, Orengo I. Mohs micrographic surgery: a treatment method for many non-melanocytic skin cancers. Dermatol Online J. 2020;26:13030/qt8zr4f9n4.
9. Kappos EA, Temp M, Schaefer DJ, Haug M, Kalbermatten DF, Toth BA. Validating facial aesthetic surgery results with the FACE-Q. Plast Reconstr Surg. 2017;139:839-45.
10. Carvalho B, Bueno R, Chahud F, Silva C. Appropriate use criteria for basal cell carcinoma Mohs surgery at a single center in the face of high-burden skin cancer: a retrospective cohort study. Journal of Dermatological Treatment. 2019;30:74-80.
11. Vaidya TS, Mori S, Khoshab N, Dusza SW, Bander T, Matros E, et al. Patient-reported aesthetic satisfaction following facial skin cancer surgery using the FACE-Q skin cancer module. Plast Reconstr Surg Glob Open. 2019;7:e2423.
12. Wang W, Lee J, Qin S, Brown MD, Doerr T. Indications and outcomes of Mohs micrographic surgery using a multidisciplinary approach: a decade of experience. Dermatol Surg. 2021;47:10-5.

Medicina CUTÁNEA Ibero-Latino-Americana

PERMANYER

Check for updates

REVIEW ARTICLE

Usefulness of dermoscopy in nail psoriasis

Utilidad de la dermatoscopia en la psoriasis ungueal

Sonia Rodríguez-Saa and Ileana R. Camardella*

Servicio de Dermatología, Hospital El Carmen, Mendoza, Argentina

Abstract

Clinical manifestations of nail psoriasis are diverse and depend on the compromised nail apparatus area. When nail involvement concomitantly occurs with skin lesions, the diagnosis is relatively easy. Nonetheless, in patients with nail compromise solely, the diagnosis is challenging. This review aims to present the current evidence on the dermatoscopic features of nail psoriasis. An exhaustive review of the literature was performed. Relevant studies published from May 2005 to May 2022 explaining the detailed dermatoscopic evaluation of the nail apparatus in patients affected with psoriasis were systematically searched for in scientific databases: Lilacs (IBECS) and PubMed. Study quality was assessed by "Quality Assessment of Diagnostic Accuracy Studies." Overall, onychoscopy is the fundamental diagnostic tool in the clinical evaluation of these patients. It is considered a non-invasive, accessible, and easy procedure during dermatoscopic visits. Onychoscopy not only confirms the clinical suspicion but also, is a useful guide for the treatment selection as it allows a complete evaluation of the nail apparatus. To conclude, we intend to emphasize the onychoscopy evaluation as a routine practice in patients affected with psoriasis and in suspected ones.

Keywords: *Psoriasis. Nail. Dermoscopy.*

Resumen

Las manifestaciones clínicas de la psoriasis ungueal son variadas y dependen del área afectada. Cuando la psoriasis ungueal ocurre concomitantemente con lesiones cutáneas, su diagnóstico es sencillo, pero en los pacientes con afectación ungueal aislada se dificulta. El objetivo de esta revisión es presentar la evidencia actual sobre las características dermatoscópicas de la psoriasis ungueal. Se realizó una revisión de las características dermatoscópicas de la psoriasis ungueal, su utilidad en el diagnóstico precoz y la relación con la gravedad de la psoriasis. Se llevó a cabo una revisión exhaustiva de la literatura científica sobre estudios que evaluaron las características dermatoscópicas de la unidad ungueal en pacientes con psoriasis. La búsqueda bibliográfica se realizó en las bases de datos Lilacs (IBECS) y PubMed desde mayo de 2005 hasta mayo de 2022. Los resultados mostraron que la onicoscopia es una herramienta útil para la evaluación del aparato ungueal, que no es invasiva y resulta rápida y accesible. En esta revisión se destacan las características dermatoscópicas clave de la psoriasis ungueal. La onicoscopia puede confirmar el diagnóstico clínico y es útil para lograr una mejor precisión diagnóstica y guiar el tratamiento adecuado, al permitir una mejor visualización de las estructuras de toda la unidad ungueal. Como conclusión, se recomienda el uso del dermatoscopio para la evaluación del aparato ungueal en la consulta dermatológica de pacientes con psoriasis.

Palabras clave: *Psoriasis. Uña. Dermatoscopia.*

***Correspondence:**
Sonia Rodríguez-Saa
E-mail: dermatodelcarmen@gmail.com

Date of reception: 05-07-2023
Date of acceptance: 05-01-2024
DOI: 10.24875/MCUTE.M24000004

Available online: 26-04-2024
Med Cutan Iber Lat Am (Eng). 2024;52(1):16-22
www.MedicinaCutaneaILA.com

Introduction

Psoriasis is a common, inflammatory, systemic, and chronic dermatosis, which is genetically based and immunologically mediated. It typically affects the skin, traditionally exhibiting erythematous and scaly lesions, with a predilection for the scalp, the lumbosacral region, and extensor surfaces of the elbows and knees. It can affect mucous membranes, semi-mucous membranes, appendages, and joints[1,2]. Nail involvement in psoriatic patients is a common finding, with a prevalence ranging from 20% up to 50% according to published studies; the prevalence in patients with psoriatic arthritis can reach up to 90%[3-5]. Nail psoriasis causes significant morbidity, with functional and esthetic impairment[1,6]. Between 5% and 10% of patients have nail involvement without skin involvement, which complicates diagnosis. Its presence is associated with a higher psoriasis area severity index (PASI), a longer course of the disease, and is an independent predictive factor for developing psoriatic arthritis[3,6].

Dermoscopy is a non-invasive diagnostic technique to examine pigmented and non-pigmented lesions. It is also useful in diagnosing nail lesions. Dermatoscopy of the nail unit is known as onychoscopy[7-9].

In this study, we conducted a review of the dermoscopic features of nail psoriasis, its utility in early diagnosis, and its relationship with psoriasis severity. The objective of this review is to present current evidence on the dermoscopic features of nail psoriasis.

Materials and methods

We conducted a comprehensive review of the scientific literature on studies evaluating the dermoscopic features of the nail unit in psoriatic patients. The literature search was performed in the Lilacs (IBECS) and PubMed databases in May 2022. The keywords “dermatoscopy” and “nail psoriasis” and their synonyms were used, both in Spanish and English ([“dermoscopy” OR “videodermoscopy” OR “dermoscopic” OR “onychoscopy”] AND [“nail psoriasis” OR “psoriatic nail”]). Articles obtained through manual search from the references of review articles were also evaluated.

The search yielded a total of 61 articles, 20 of which were excluded due to duplication. Then, 23 articles were excluded for not being original studies or being irrelevant. Original articles that included the dermoscopic description of nail psoriasis as a primary topic, in English and Spanish, were included for review. Information from the 18 selected articles was collected, summarized, organized, and edited through narrative synthesis.

Results

Onychoscopy can be performed with a manual dermatoscope providing a 10× magnification or with a digital dermoscopy system for the acquisition of images with higher magnification (between 20× and 70×); both allow saving images for subsequent monitoring. It is recommended to perform dry onychoscopy first and then apply ultrasound gel or gel alcohol to the target region, which, due to its viscosity, remains on the surface and fills the space between the convex surface of the nail and the flat surface of the dermatoscope[10,11]. To avoid compression of capillaries and improve their visualization, dermoscopy with polarized light and without contact is recommended[12].

Onychoscopy allows better visualization of anomalies that may be clinically observed and facilitates the detection of early or mild changes[4,13].

Yadav and Khopkar 14 performed dermoscopy on 68 patients with chronic plaque psoriasis, with subtle nail lesions not easily discernible to the naked eye. They found that 46 exhibited dermoscopic changes. The most common and statistically significant findings compared to healthy controls were pits, distal and lateral onycholysis, oil drop sign, splinter hemorrhage, and the presence of dilated vessels in the onychoderm band surrounded by a pale halo[14].

The clinical signs of nail psoriasis are varied and depend on the affected region; the nail bed, nail matrix, hyponychium, and nail folds can be compromised. Table 1 illustrates the most common clinical signs according to the location of the disease[6]. These characteristics are not exclusive to psoriasis but are useful for its diagnosis.

Dermoscopic findings of nail matrix involvement

Signs of nail matrix involvement in psoriasis include pits, leukonychia, red spots in the lunula, dystrophy (fragility and disintegration of the nail plate), transverse grooves, and trachyonychia (rough nails with a dull appearance due to the presence of longitudinal striations and pinpoint depressions)[6].

Pits (Fig. 1) are caused by defective keratinization of the proximal nail matrix, leading to the accumulation of para-keratotic cell foci. Shedding of these cell foci results in the formation of pinpoint depressions in the nail plate[15]. Pits are best observed with dry onychoscopy and in nail psoriasis, they are characterized by being deep, irregular in shape, size, and distribution, sometimes covered with scales and a white halo[7,14,16,17].

Table 1. Clinical characteristics of nail psoriasis based on the region that has been damaged

Localization of damage	Clinical finding	Description
Nail matrix	Pits	Small depressions in the nail plate
	Leukonychia	White discoloration of the nail plate
	Red spots in the lunula	Pink-red dotted areas in the lunula
	Nail plate disintegration	Fragility and disintegration of the nail plate, nail dystrophy
	Beau's lines	Transverse grooves in the nail plate
	Trachyonychia	Rough and dull nails, with abundant longitudinal streaks and pinpoint depressions
Nail bed	Splinter hemorrhages	Linear areas of visible bleeding through the nail plate
	Onycholysis	Distal separation of the nail plate from the nail bed
	Oil spots or salmon patches	Irregular areas of yellowish or salmon-colored pigmentation
	Subungual hyperkeratosis	Accumulation of white-grayish keratin between the bed and the nail plate
Hyponychium	Onychorrhexis	Longitudinal ridges and distal splitting of the nail plate

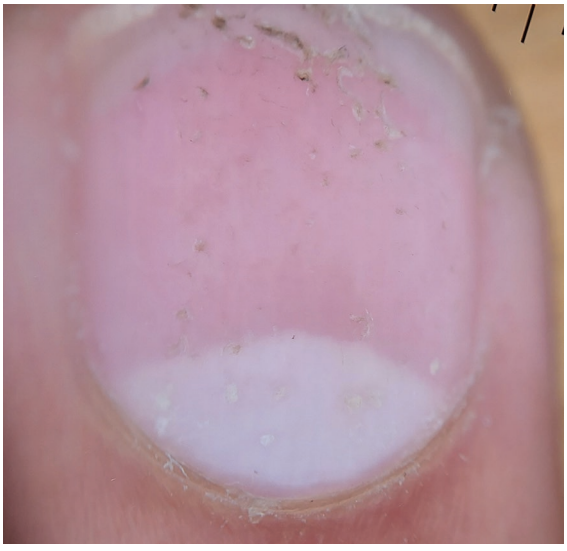


Figure 1. Pits.

In the study by Chauhan et al.[10], pits were the most common finding, present in 60.5% of the fingers of the hands and only 5.9% of the toes. Similar results have been reported in other studies[1,4,12,15].

Leukonychia occurs due to para-keratosis of the distal nail matrix, which prevents the normal shedding of underlying keratinocytes. A slightly higher frequency of leukonychia has been observed through dermoscopic examination versus clinical observation[15].

Longitudinal striations were found in 57.3% of the fingers of the hands and 22.7% of the toes, and leukonychia in 26.4% of the fingernails and 11.8% of the toenails, which was similar to the naked-eye examination, and nail plate dystrophy in approximately 22% of the fingernails and 82% of the toenails. Similar results were obtained in other studies[1,4,12,15,18,19].

A red spot in the lunula or red lunula is an infrequent finding. With onychoscopy, the detection of this finding increased from 0.2% up to 12.9% in the nails of the hands and from 0% to 3.9% in the nails of the feet clinically involved. Among clinically uninvolved nails, this finding was evident in 18/107 (16.8%) in the hands and 10/339 (2.9%) in the feet. Red spots in the lunula were described in only 1.5% to 8% of cases[1,10,15].

In the study by Long et al.[12], they found that 83.3% of nails with a red lunula were accompanied by dilated linear capillaries. Histopathologically, the red lunula corresponds to an increased blood flow.

Blurry lunula was an additional finding reported in the work of Chauhan et al.[10], described as a wide, white, and irregular lunula, which had not been previously reported in the literature. In clinically affected nails, it was observed in 33.6% of the fingernails and 4.9% of the toenails. In clinically unaffected nails, it was observed in 8.4% of the fingernails and 1.8% of the toenails[10].

Dermoscopic findings of nail bed involvement

Signs of nail bed involvement in psoriasis include subungual hyperkeratosis, dilated capillaries, onycholysis, splinter hemorrhages, and oil drop (or salmon patch)[6].

In both fingernails and toenails, subungual hyperkeratosis (Fig. 2) is the most common feature: 52.8% of fingernails and 85.1% of toenails. Its observation increased by 40% and 73%, respectively, compared to the naked eye examination. Other authors found lower frequencies, ranging from 9% up to 46%[10,14,15].

In approximately 50% of fingernails and 10.8% of toenails, dilated capillaries of bright red or dark red color surrounded by a pale halo in the onychodermal band were found. This finding was also present in 28% of clinically unaffected fingernails and 2.4% of clinically unaffected toenails. Furthermore, Yadav and Khopkar 14 reported their presence in 19.5% of cases, and Long et al. in 60%[12].

Onycholysis (Fig. 3) occurs due to the separation of the nail plate from the nail bed and is observed in onychoscopy as an opaque area in the distal or lateral part of the nail plate. It is one of the most common findings in nail psoriasis, found in up to 93.3% of cases in some studies[1,10,12-15].

Yorulmaz and Artuz1 observed a linear erythematous border around onycholysis at its proximal end, which was better observed with dermoscopy versus clinical examination. This finding cannot be seen in traumatic onycholysis or onychomycosis, making it specific to psoriatic nails and useful for the diagnosis of nail psoriasis, especially in cases of isolated onycholysis. Its approximate frequency is 22%[1,7,12,13,15].

Splinter hemorrhages (Fig. 4) are also a common finding, although less specific to nail psoriasis. They appear as thin, longitudinal lines, usually in the distal part of the nail, red or purple when recent, and over time become reddish-brown and darker. They are caused by capillary rupture, which in this location runs longitudinally in the dermoepidermal ridges, causing blood extravasation beneath the nail plate, giving it a linear or "splinter" appearance[1,14,17].

Onychoscopy improves the visualization of splinter hemorrhages, which can also be seen with greater magnification as pinpoint or elongated serpentine hemorrhages[1,7,15]. Onychoscopy increased their detection by 20% up to 40% in fingernails and from 21% up to 31% in toenails[1,10,12-15].

Oil spots or salmon patches are irregular translucent areas of yellowish-red or orange color; they appear red in dark skin. They occur due to focal onycholysis due to para-keratosis of the nail bed[1,7,17]. They have been reported in 10% of fingernails and 2.9% of toenails. The lower frequency of oil spots in toenails versus fingernails may be attributed to increased dystrophy in the toenails, making the visualization of oil spots difficult even on the onychoscopy[1,10,14,15].

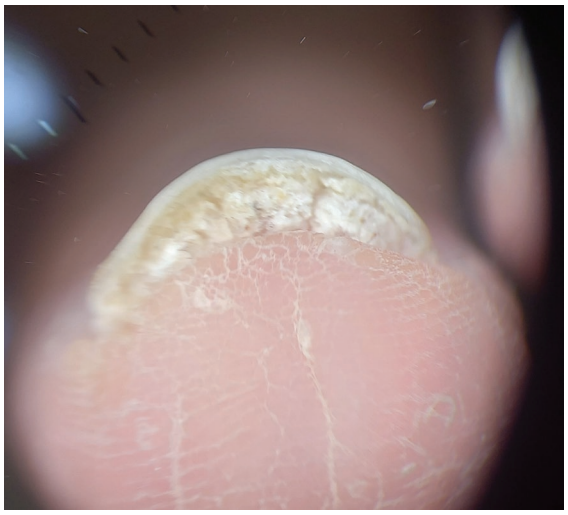


Figure 2. Subungual hyperkeratosis.

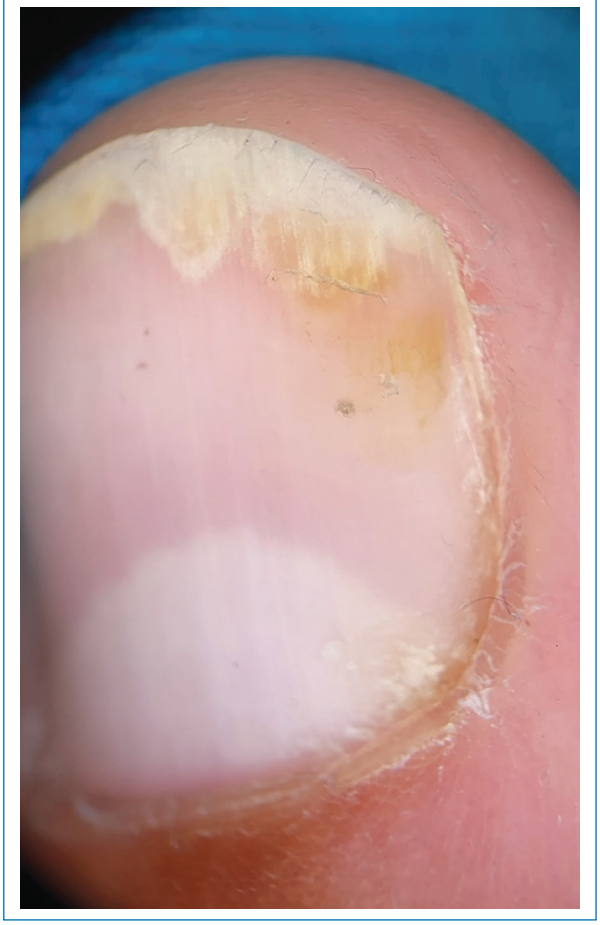


Figure 3. Distal onycholysis with erythematous border.

The pseudofiber sign (Fig. 5) was first described by Yorulmaz and Artuz[1], who observed this characteristic on

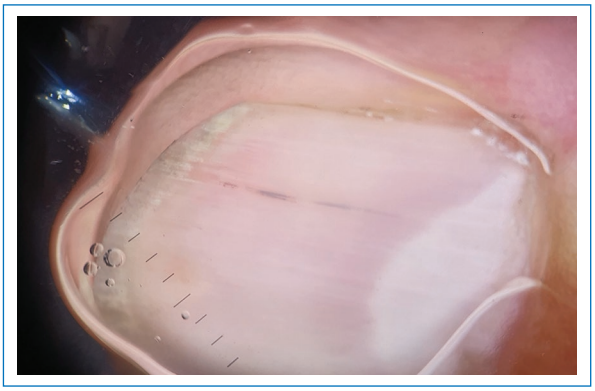


Figure 4. Splinter hemorrhage.

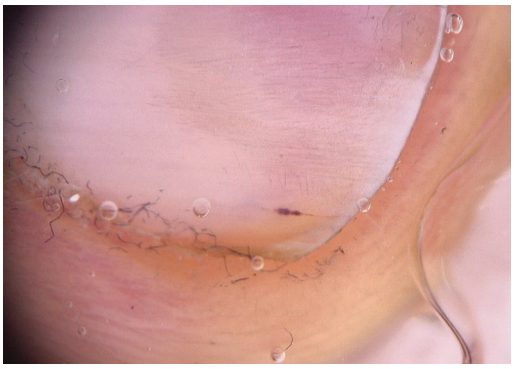


Figure 5. Textile fibers beneath the nail plate and dilated capillaries in the hyponychium.

the dermoscopy in 34.3% of their patients. Pseudofibers are filamentous structures of red and black color, located near the cuticle or under the hyponychium along the free distal edge of the nail plate. They suggested that the pseudofiber sign might be related to psoriasis of the nail bed and that filamentous structures represent bare capillaries. This hypothesis has been questioned by several authors. Ankad et al.[7] consider this sign analogous to the "textile fiber" described by Lencastre et al., in which fibers adhere to an excoriated or ulcerated surface, and they also observed that these structures could be easily removed, so they represent tissue fibers rather than the venous or arterial ends of capillaries. Therefore, they suggest not using the prefix "pseudo." In their study[20], reported the presence of adherent textile fibers in 34.2% of patients with nail psoriasis.

Dermoscopic findings in the hyponychium

The hyponychium can be observed by placing the dermatoscopy underneath the free edge of the nail plate[17]. Hyponychial onychoscopy is very useful to confirm the diagnosis of psoriasis in patients presenting solely with onycholysis or mild subungual hyperkeratosis. Irregularly distributed, dilated, tortuous, and elongated capillaries can be observed[17,21]. Capillaries are best visualized at 40× magnification; at lower magnification with a manual dermatoscope, they may appear as regular red dots[1,17,21,22]. This sign could be due to underlying changes to dermal vasculature, which may be representative of the well-described Auspitz sign clinically demonstrated in psoriatic plaques[15].

Hyponychial onychoscopy of clinically affected nails showed regularly arranged red dots in 38.6% of fingernails and 59.4% of toenails, and dilated, tortuous, and irregular capillaries in 2.9% of fingernails and 0.9% of toenails. In addition, onychoscopy was able to detect similar changes in clinically unaffected fingers and toenails (34.6% vs. 5.6%)[10]. In the study conducted by Ankad et al.[7], red dots in the hyponychium were the most common finding. This was reported in 35.8% of cases by Yorulmaz and Artuz[1], and in 10% of cases by Wanniang et al.[15], while Iorizzo et al.[21] reported this finding in the 30 patients with nail psoriasis from their study.

Hyponychial onychoscopy can also be a useful supportive tool for differentiating early psoriatic arthritis from early rheumatoid arthritis. The differential diagnosis of these two diseases can be quite difficult, as both can present with symmetric joint involvement. In early psoriatic arthritis, dermatoscopy shows diffuse distribution of pinpoint red vessels. In rheumatoid arthritis, three vascular patterns may be observed: (1) irregular, blurry, purple vessels; (2) avascular appearance; or (3) scattered, pinpoint, purple vessels[17,23,24].

Correlation with disease severity and treatment response

According to the study by Iorizzo et al.[21], hyponychial capillary density correlates positively with disease severity. Yorulmaz and Artuz1 evaluated 67 patients with nail psoriasis and found that the pseudofiber sign, dilated capillaries in the hyponychium, nail dystrophy, subungual hyperkeratosis, transverse grooves, and trachyonychia were positively associated with the severity of nail psoriasis. Similar results were obtained in the study by Long et al.[12], where red lunulae, longitudinal ridges, and erythematous borders of onycholytic areas correlated with the severity of nail psoriasis.

The study by Arora et al.[4] they calculated the nail psoriasis severity index (NAPSI) and modified

NAPSI (mNAPSI) using the dermatoscopy (dNAPSI and dmNAPSI), and found that it improved the detection of early psoriasis and that dNAPSI was better than NAPSI at detecting worsening of PASI in moderate-to-severe psoriasis. Both mNAPSI and dmNAPSI increased with the severity of joint involvement, with no significant differences reported between these two indices.[4]

Onychoscopy can be useful for assessing treatment response, although research in this area is currently limited. Iorizzo et al.[21] reported fewer visible hyponychial capillaries after 3 months of treatment with calcipotriol ointment twice daily. Hashimoto et al.[19] observed that the resolution of diffuse nail plate scaling, transverse fissures, nail plate thickening, and splinter hemorrhages were associated with improvements in patients' PASI after biological treatment.

Utility in the differential diagnosis

Red dots on the hyponychium do not seem to be associated with onycholysis due to onychomycosis or trauma. This means that the red dots would be specific to onycholytic psoriasis[7].

Dermoscopy of nail pits can be useful for differential diagnosis with other diseases that also exhibit these signs, especially when they are the only sign of nail psoriasis. The other common disease that can present solely with nail pits is alopecia areata, but in this disease, they are regular in shape, size, and distribution[17].

Dermoscopy helps clinically differentiate onycholysis based on different etiologies. In their study, Ankad et al.[7] found that onycholysis due to psoriatic nails, distal and lateral onychomycosis, and trauma, exhibits distinctive and characteristic onychoscopic patterns. The serrated proximal edge, the northern lights sign, and the "ruined" pattern of subungual hyperkeratosis are specific features of onychomycosis. In traumatic onycholysis, the history of trauma is very useful, but in many cases, the patient does not remember it, so dermatoscopy is very helpful, since in traumatic onycholysis the proximal edge is linear, regular, and smooth, not surrounded by an erythematous border as occurs in psoriasis-induced onycholysis[7,19].

Discussion

When nail psoriasis occurs concomitantly with skin lesions, its diagnosis is straightforward, but in patients with isolated nail involvement, it becomes difficult due to its similarity with other causes, such as onychomycosis, lichen planus, alopecia areata, pityriasis rubra pilaris, traumatic onycholysis, and others. Nail biopsy is the method of choice for diagnosis, but it is painful, can leave a scar or permanent changes to nail growth, and has proven diagnostic only in 50% of cases of nail psoriasis. Onychoscopy can serve as a tool to improve diagnosis and could avoid biopsy in some cases[10].

Onychoscopy is useful for evaluating the nail apparatus and is non-invasive, quick, and accessible. In this review, we highlighted the key dermoscopic features of nail psoriasis. After evaluating the published studies, a great heterogeneity in the terminology used emerges, making comparison difficult.

Onychoscopy acts as a bridge between clinical and histopathological examinations and helps diagnose nail psoriasis even before the appearance of clinical signs of nail involvement. The presence of dermoscopic features in clinically unaffected nails can serve as an early marker of disease activity.

Conclusions

Onychoscopy is a useful tool for evaluating the nail apparatus. Onychoscopy can confirm clinical diagnosis and is useful for achieving better diagnostic accuracy and guiding appropriate treatment, by allowing a better visualization of nail structures as a whole. Although histopathology provides definitive information, there is a good correlation between clinical, dermoscopic, and histopathological examinations in the differential diagnosis of nail diseases.

Based on the results of this review, the use of a dermatoscope is recommended for evaluating the nail apparatus in the dermatological consultation of patients with psoriasis.

Funding

The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code

of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appears in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Yorulmaz A, Artuz F. A study of dermoscopic features of nail psoriasis. Postepy Dermatol Alergol. 2017;34:28-35.
2. Consenso Nacional de Psoriasis. Guía de Tratamiento. Actualización 2020. Buenos Aires, Argentina: Sociedad Argentina de Dermatología; 2020. Disponible en: https://sad.org.ar/wp-content/uploads/2020/08/CONSENSO-NACIONAL-DE-PSORIASIS.-ACTUALIZACION-2020.pdf.
3. Lim SS, Chamberlain A, Hur K, Ohn J, Han B, Mar V, et al. Dermoscopic evaluation of inflammatory nail disorders and their mimics. Acta Derm Venereol. 2021;101:adv00548.
4. Arora S, Paul D, Kumar R, Bhatnagar A, Arora G, Mech S, et al. Study of nail psoriasis and dermoscopic correlation with dermoscopic and modified dermoscopic nail psoriasis severity indexes (dNAPSI and dmNAPSI). Dermatol Pract Concept. 2022;12:e2022010.
5. Ortner VK, Mandel VD, Bertugno S, Philipsen PA, Haedersdal M. Imaging of the nail unit in psoriatic patients: a systematic scoping review of techniques and terminology. Exp Dermatol. 2022;31:828-40.
6. Canal-García E, Bosch-Amate X, Belinchón I, Puig L. Psoriasis ungueal. Actas Dermo-Sifiliográficas. 2022;113:481-90.
7. Ankad BS, Gupta A, Alekhya R, Saipriya M. Dermoscopy of onycholysis due to nail psoriasis, onychomycosis and trauma: a cross sectional study in skin of color. Indian Dermatol Online J. 2020;11:777-83.
8. Farias DC, Tosti A, Chiacchio ND, Hirata SH. Aspectos dermatoscópicos na psoríase ungueal. An Bras Dermatol. 2010;85:101-3.
9. Golińska J, Sar-Pomian M, Rudnicka L. Dermoscopic features of psoriasis of the skin, scalp and nails — a systematic review. J Eur Acad Dermatol Venereol. 2019;33:648-60.
10. Chauhan A, Singal A, Grover C, Sharma S. Dermoscopic features of nail psoriasis: an observational, analytical study. Skin Appendage Disord. 2020;6:207-15.
11. Fernández Pugnaire MA, Serrano Falcón C, Serrano Ortega S. Exploración de las uñas con dermoscopia: onicoscopia. Med Cutan Iber Lat Am. 2013;41:151-60.
12. Long F, Zhang Z, He F, Tu J, Yin Z, Xia J, et al. Dermoscopic features of nail psoriasis: positive correlation with the severity of psoriasis. J Dermatol. 2021;48:894-901.
13. Ayşegül P, Kapıcıoğlu Y. Dermoscopic findings of psoriatic nail and their relationship with disease severity. Turkderm. 2017;51:119-23.
14. Yadav TA, Khopkar US. Dermoscopy to detect signs of subclinical nail involvement in chronic plaque psoriasis: a study of 68 patients. Indian J Dermatol. 2015;60:272-5.
15. Wanniang N, Navya A, Pai V, Ghodge R. Comparative study of clinical and dermoscopic features in nail psoriasis. Indian Dermatol Online J. 2020;11:35-40.
16. Abu El-Hamd M, Yassin FESE, El-Hamid NHA, El-Sharkawy REED. Clinical, dermoscopic, and histopathological evaluations of patients with nail disorders. J Cosmet Dermatol. 2022;21:347-57.
17. Starace M, Alessandrini A, Piraccini BM. Dermoscopy of the nail unit. Dermatol Clin. 2021;39:293-304.
18. You Z, Yang H, Ran Y. Clinical parameters associated with severity of nail psoriasis and therapeutic efficacy. Eur J Dermatol. 2020;30:362-71.
19. Hashimoto Y, Uyama M, Takada Y, Yoshida K, Ishiko A. Dermoscopic features of nail psoriasis treated with biologics. J Dermatol. 2017;44:538-41.
20. Lencastre A, Pinheiro R, Cunha N. A study of dermoscopic features of nailpsoriasis: the pseudo-pseudo-fiber sign. Postepy Dermatol Alergol. 2018;35:649.
21. Iorizzo M, Dahdah M, Vincenzi C, Tosti A. Videodermoscopy of the hyponychium in nail bed psoriasis. J Am Acad Dermatol. 2008;58:714-5.
22. Lencastre A, Lamas A, Sá D, Tosti A. Onychoscopy. Clin Dermatol. 2013;31:587-93.
23. Errichetti E, Zabotti A, Stinco G, Quartuccio L, Sacco S, De Marchi G, et al. Dermoscopy of nail fold and elbow in the differential diagnosis of early psoriatic arthritis sine psoriasis and early rheumatoid arthritis. J Dermatol. 2016;43:1217-20.
24. Zabotti A, Errichetti E, Zuliani F, Quartuccio L, Sacco S, Stinco G, et al. Early psoriatic arthritis versus early seronegative rheumatoid arthritis: role of dermoscopy combined with ultrasonography for differential diagnosis. J Rheumatol. 2018;45:648-54.

Medicina CUTÁNEA Ibero-Latino-Americana

PERMANYER

Check for updates

CASE REPORT

Case series, clinical spectrum of cutaneous leishmaniasis in a family: another great imitator

Serie de casos, espectro clínico de la leishmaniasis cutánea en una familia: otro gran imitador

Mauricio Torres-Pradilla, Nicolle Guiot-Isaac, and Samuel Morales*

Dermatología FUCS/HSJ, Fundación Universitaria de Ciencias de la Salud, Hospital San José, Bogotá, Colombia

Abstract

Leishmaniasis is a parasitic disease endemic in Central and South America. There are three main clinical forms: cutaneous, mucocutaneous, and visceral leishmaniasis, with a variable prognosis. Diagnosis is made based on clinical features, epidemiological context, and parasitological confirmation. To report the cases of three family members: a 42-year-old father, his 13-year-old daughter, and his 6-year-old son, with different clinical manifestations of cutaneous leishmaniasis, some of which resemble other cutaneous diseases. Case series. The clinical spectrum of cutaneous leishmaniasis is broad. Therefore, it is necessary to maintain a high level of clinical suspicion to do early diagnosis and offer an optimal treatment.

Keywords: *Leishmaniasis. Cutaneous leishmaniasis. New world leishmaniasis.*

Resumen

La leishmaniasis es una enfermedad parasitaria endémica en países de Centroamérica y Sudamérica. Existen tres formas clínicas principales: leishmaniasis cutánea, mucocutánea y visceral, con un pronóstico variable. El diagnóstico se basa en la clínica, el contexto epidemiológico y la confirmación parasitológica. Reportar tres casos de leishmaniasis cutánea en una familia: el padre de 42 años, su hija de 13 años y su hijo de 6 años. Presentaban lesiones diferentes, atípicas, que imitaban otras enfermedades dermatológicas. Serie de casos. La presentación clínica de la leishmaniasis cutánea es amplia. Se debe mantener una alta sospecha clínica para poder realizar un diagnóstico temprano y emplear un tratamiento oportuno.

Palabras clave: *Leishmaniasis. Leishmaniasis cutánea. Leishmaniasis del Nuevo Mundo.*

Introduction

Leishmaniasis is an endemic parasitic infection in Colombia and therefore represents a problem for public health. It has been found more frequently in Guaviare, Nariño, and Risaralda[1]. There are three clinical forms of leishmaniasis: cutaneous, mucocutaneous, and visceral. Cutaneous leishmaniasis usually presents as a papule or nodule that ulcerates, with subsequent self-resolution in most cases[2]. However, uncommon forms have been described whose clinical presentation poses a diagnostic challenge, as it can mimic or resemble other skin diseases[3]. Within the atypical lesions, eczematous, psoriasiform, lupoid, and sporotrichoid lesions have been described, among others.

***Correspondence:**
Nicolle Guiot-Isaac
E-mail: nguiot@fucsalud.edu.co

Date of reception: 11-05-2023
Date of acceptance: 24-10-2023
DOI: 10.24875/MCUTE.M24000006

Available online: 26-04-2024
Med Cutan Iber Lat Am (Eng). 2024;52(1):23-27
www.MedicinaCutaneaILA.com

We present the case reports of the members of the same family with different clinical presentations of cutaneous leishmaniasis treated at the dermatology department of the Hospital de San José in Bogotá, Colombia. These cases demonstrate the wide spectrum of clinical signs of cutaneous leishmaniasis, constituting a diagnostic challenge.

Case reports

Three members of a family presented to the dermatology department of the hospital de San José. The father, aged 42, consulted with his 13-year-old daughter and 6-year-old son due to the presence of erythematous, pruritic, progressively growing lesions with ulceration following a trip to a rural area of Boyacá 3 months prior. The morphology of the lesions and the affected location varied among the three cases. None of them had a relevant past medical history.

On physical examination, the child exhibited an erythematous, ulcerated plaque with infiltrated erythematous edges and a clean center, located in the periumbilical region (Fig. 1). In the girl, multiple infiltrated erythematous plaques with desquamation, a few verrucous areas, and others ulcerated with hematic crusts were observed on the arms, resembling eczematous disease (Fig. 2). Finally, the adult exhibited an infiltrated tumoral lesion on his right cheek, resembling a lupoid lesion (Fig. 3). None of them exhibited mucosal changes or lymphadenopathies.

Considering the clinical characteristics and the epidemiological context, cutaneous leishmaniasis was suspected. Skin biopsies were performed, with similar histopathological findings in all three cases. Normal epidermis was observed with a nodular and diffuse infiltrate in the dermis composed of lymphohistiocytes and numerous plasma cells. Given this, the histopathological diagnosis was nodular granulomatous dermatitis rich in plasma cells of infectious etiology.

Considering the clinical characteristics and the epidemiological context, cutaneous leishmaniasis was suspected. Skin biopsies were performed, with similar histopathological findings in all three cases. A normal epidermis was observed with a nodular and diffuse infiltrate in the dermis composed of lymphohistiocytes and numerous plasma cells (Fig. 4). Therefore, the histopathological diagnosis was nodular granulomatous dermatitis rich in plasma cells of infectious etiology.

Considering the history of recent travel exposure to an endemic area, the clinical features, and histopathology, the diagnosis of cutaneous leishmaniasis was established in all three cases. The two pediatric patients received oral miltefosine at a dose of 2.5 mg/kg/day for 28 days. The father received intramuscular meglumine at a dose of 20 mg/kg/day for 20 days. At 3 months, all three patients showed a 90% clinical response, without sequelae (Fig. 5).

Given the variety of clinical presentations of cutaneous leishmaniasis seen in our patients, mainly atypical, we present these cases below, plus a brief review of the literature.

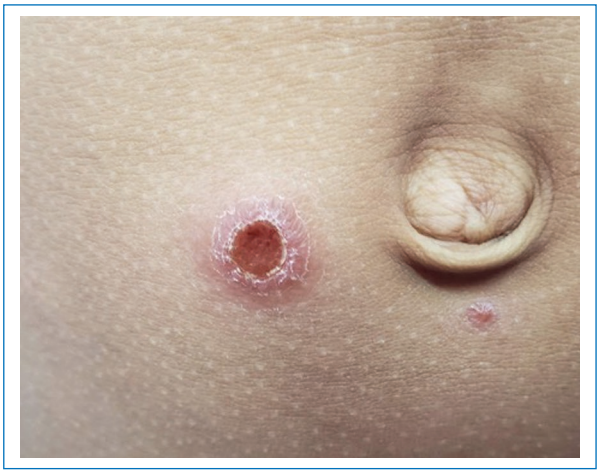


Figure 1. Typical presentation in the child in the periumbilical region showing an erythematous, ulcerated plaque with raised, infiltrated edges, a clean base, and in the infraumbilical region showing an erythematous papule.

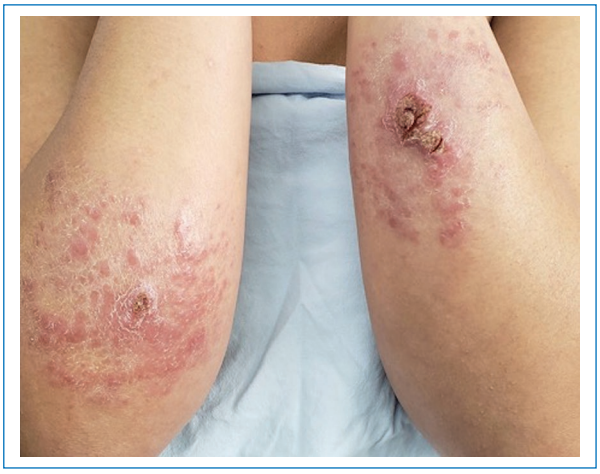


Figure 2. Atypical presentation in the adolescent patient. On the arms, multiple erythematous, infiltrated plaques with desquamation, some verrucous areas, and others ulcerated with hematic crusts, resembling eczematous disease can be seen.

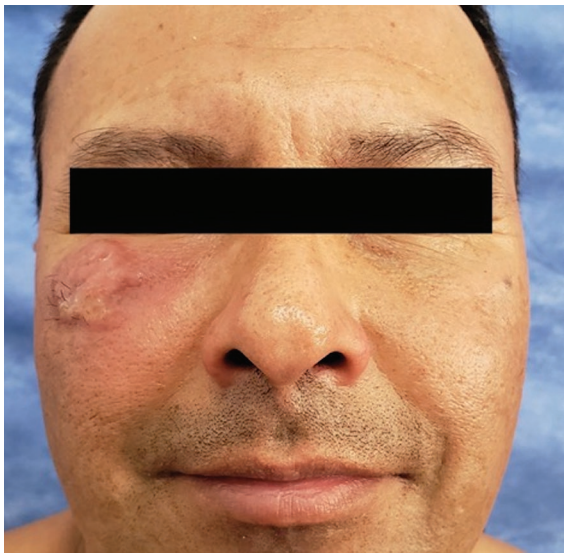


Figure 3. Atypical presentation in the adult patient. On the right cheek, a tumoral, erythematous, infiltrated plaque with a lupoid appearance can be seen.

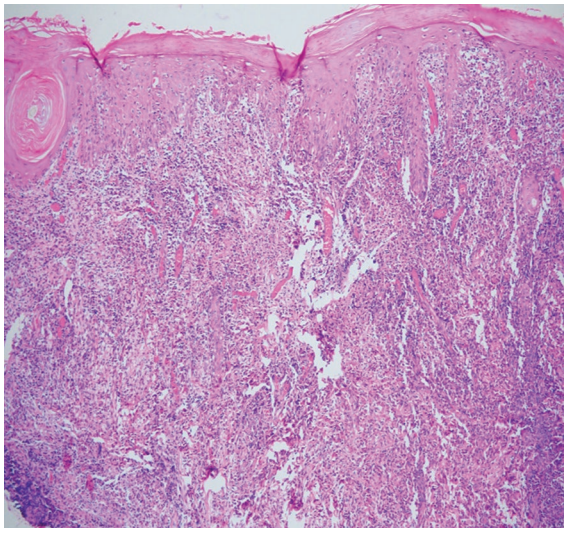


Figure 4. Histopathological findings. Nodular and diffuse infiltrate in the dermis composed of lymphohistiocytes and numerous plasma cells.

Discussion

Leishmaniasis is a parasitic infection that results in a wide spectrum of diseases. There are three main clinical forms of leishmaniasis: cutaneous, mucocutaneous, and visceral. Given the different forms of presentation, severity can vary from mild to potentially fatal[4].

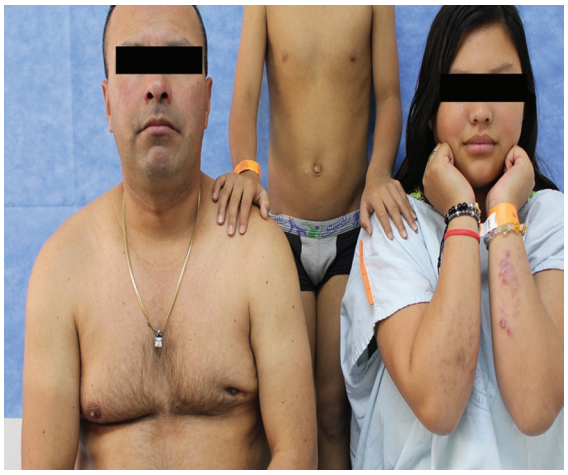


Figure 5. Clinical response after treatment. Note the clinical improvement.

The parasites of Leishmania causing cutaneous leishmaniasis are divided into two groups: Old World (*Leishmania major*, *Leishmania tropica*, and *Leishmania aethiopica*) and New World species (*Leishmania amazonensis*, *Leishmania mexicana, Leishmania brasiliensis*, and *Leishmania guyanensis*). The latter are endemic in Central America and South America[2].

Leishmaniasis is primarily a zoonotic disease, meaning it is transmitted from animals to humans. Sandflies belonging to the genus *Phlebotomus* (Old World) or *Lutzomyia* (New World) transmit the parasite. The vector takes blood and regurgitates promastigotes into human skin, which are then phagocytosed by macrophages. Within these cells, promastigotes transform into amastigotes, non-flagellated intracellular forms, which then multiply and cause the disease. The immune response directed by helper T cells 1 (Th1) and 2 (Th2) can control the infection and even achieve self-resolution in most cases[4].

The World Health Organization estimates 0.7-1 million cases of cutaneous leishmaniasis annually, affecting individuals worldwide. More than 60 countries are listed as endemic areas, with the majority in Central and South America. In Colombia, in 2018, 6426 cases of leishmaniasis were reported, mainly in Guaviare, followed by Nariño and Risaralda. A total of 98.3% (6319) of cases corresponded to the cutaneous form of the disease[1]. In order of frequency, cutaneous leishmaniasis is the most common one, followed by mucocutaneous and visceral. It is estimated that there are more than 11 million people at risk in Colombia. Therefore, it is considered a public health problem[5].

Back in 2019, Valero and Uriarte[6] conducted a literature review of the social, environmental, and climatic factors associated with leishmaniasis and sought to determine their impact on the incidence of the disease. Socioeconomic and demographic factors were significant in 49% of cases of cutaneous leishmaniasis. Low economic level and related factors such as poverty (lack of hygiene, malnutrition, poor conditions), presence of animals in the environment, work or residence in rural areas, and lack of protection measures against bites are considered important risk factors for cutaneous leishmaniasis (67%). Climatic variables also constituted a risk factor. A mean temperature of 16 ± 5.7°C was found in all areas, with the highest incidence in the Andean region of Colombia[6]. Therefore, the epidemiological context is a key clue to diagnostic suspicion.

Cutaneous leishmaniasis is classified as acute or chronic, depending on whether lesions last for more than 1 year[7]. Most lesions are typical and diagnosed rapidly. A few weeks or months after the bite, papules or nodules develop, progressively growing until ulceration occurs. The ulcer is characterized by raised edges and a clean center, resolving within a period of 3-18 months. However, it is estimated that 10% of cases progress, become chronic, and present more severe clinical signs[2].

Apart from the typical clinical form, it can also present with a wide variety of atypical cutaneous lesions, making it a "great imitator" disease. In these cases, diagnosis can be difficult to establish and often delayed. Atypical clinical lesions can manifest in various forms, such as erysipelas-like, sporotrichoid, eczematous, lupoid, verrucous, chancroid, acneiform, or psoriasiform lesions, among others[3]. These atypical forms tend to occur mainly in cases of chronic cutaneous leishmaniasis[7].

Several factors contribute to the different morphologies of the chronic form of the disease, such as parasite species, virulence, host immunity, and geographic factors[3]. Regarding the immune response, it is associated with an imbalance between the Th1 and Th2 responses, i.e., a decrease in the Th1 response and a predominance of the Th2 response. Therefore, there is a decrease in interleukin (IL) 1α, IL-6, transforming growth factor-beta (TGF-β), interferon-gamma, and tumor necrosis factor-alpha, and on the other hand, there is increased production of the cytokines IL-4, IL-5, TGF-β, and IL-10.

Of the three cases presented here, two exhibited atypical lesions. The adolescent developed the eczematous form, which can manifest as acute dermatitis with vesicular lesions, exudate, crusts, or, rarely, chronic eczematous lesions that are often found on the extremities. It has been postulated that this clinical presentation is due to a severe imbalance in cellular immunity, although this was not the case in our patient. On the other hand, the father had a lesion mimicking discoid lupus erythematosus. It usually manifests as atrophic plaques with central scaling and peripheral papules. Granulomatous dermatitis is observed in histopathology instead of interface dermatitis[3].

It is important to recognize and treat this disease promptly, as it can lead to permanent scarring, affect quality of life, and stigma[2].

Diagnosis is based on clinical features and epidemiological context, but definitive parasitic confirmation is necessary. It is recommended to combine different tests, such as histopathological examination, smears, culture, and, if possible, DNA amplification techniques[1].

Histopathological examination may show different findings, such as abundant amastigotes, called Leishman-Donovan bodies, present in approximately 45% of cases, with sensitivity rates of 50% up to 70%. Other findings include a mixed infiltrate composed of macrophages, neutrophils, and plasma cells with necrosis (27.5%), early granuloma formation with focal collection of epithelioid cells, lymphocytes, and some plasma cells (15%), and lastly, less frequently (5%), epithelioid granulomas in the dermis with Langerhans giant cells, lymphocytes, and epithelioid cells[8].

On the other hand, the parasite can only be identified in 70% of cases of cutaneous leishmaniasis. Culture is the best method to isolate it, but it is costly and time-consuming (approximately 2 weeks). Another recommended method is the smear, which has the advantage of being economical, simple, and rapid for diagnosis. Finally, polymerase chain reaction, although it has high sensitivity and allows determination of specific *Leishmania* species, is costly, and its availability is a significant limitation, as in our environment[8].

As mentioned, cutaneous lesions tend to resolve spontaneously. The decision to initiate treatment aims to accelerate healing and reduce scarring and the risk of dissemination or progression. To choose the appropriate treatment, the patient's age and immune status, the involved species, and the geographic area where the infection was contracted should be considered. Therefore, treatment should be individualized in each particular case[2].

In the management of a patient with cutaneous leishmaniasis, three possible scenarios should be considered: (1) observation and follow-up, (2) local treatment,

and (3) systemic treatment. Observation and expectant management may be indicated in patients with simple cutaneous leishmaniasis lesions in spontaneous resolution at the time of diagnosis and without mucous membrane involvement. Local treatment is generally indicated for simple lesions, i.e., scarce, small lesions that do not cause functional or esthetic changes. Finally, systemic treatment is indicated in cases of simple cutaneous leishmaniasis that do not respond to local therapy and in cases of complicated cutaneous leishmaniasis[9].

Some possible options for local therapies include thermotherapy, cryotherapy, electrosurgery, surgical excision, curettage, radiofrequency, or topical compounds such as imiquimod, paromomycin, or trichloroacetic acid. Systemic treatments include pentavalent antimonials (meglumine), miltefosine, amphotericin B, pentamidine, and azoles (itraconazole, fluconazole, and ketoconazole)[9].

The first-line therapy for cutaneous leishmaniasis in adults is pentavalent antimonials (meglumine 20 mg/kg/day for 20 days), and for pediatric cases, oral miltefosine (2.5 mg/kg/day for 28 days). Other options for special or refractory cases include liposomal amphotericin B and pentamidine[1,8].

Conclusions

In conclusion, we presented three cases with different clinical lesions of cutaneous leishmaniasis: lupoid form, eczematous form, and typical presentation. Since Colombia is an endemic country for leishmaniasis, it is important to know the wide spectrum of clinical presentation of this disease, including typical and atypical forms, to avoid misdiagnosis and ensure timely treatment.

Acknowledgments

The authors wish to thank Dr. Myrna Gómez and Dr. Juliana Cáceres, graduates of Dermatology from FUCS, and the Dermatology editorial committee, especially Dr. María Paula Gutiérrez, for their collaboration.

Funding

The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript or for the creation of images, graphics, tables, or their corresponding captions.

References

1. Agudelo N. Instituto Nacional de Salud. Minsalud. Informe del evento. Leishmaniasis cutánea, mucosa y visceral Colombia 2018; version: 04: p. 1-28. Disponible en: https://www.ins.gov.co/buscador-eventos/Informesdeevento/LEISHMANIASIS_2018.pdf.
2. Burza S, Croft SL, Boelaert M. Leishmaniasis. Lancet. 2018;392:951-70.
3. Gurel MS, Tekin B, Uzun S. Cutaneous leishmaniasis: a great imitator. Clin Dermatol. 2020;38):140-51.
4. Mokni M. [Cutaneous leishmaniasis]. Ann Dermatol Venereol. 2019;146:232-46.
5. Grupo de Enfermedades Transmisibles Endoepidémicas y Relacionadas con Salud Sexual. Instituto Nacional de Salud. Minsalud. Protocolo de Vigilancia de Leishmaniasis. 2022 Versión: 05.p.1-28.Disponible en: https://www.ins.gov.co/buscadoreventos/Lineamientos/PRO_Leishmaniasis.pdf.
6. Valero NNH, Uriarte M. Environmental and socioeconomic risk factors associated with visceral and cutaneous leishmaniasis: a systematic review. Parasitol Res. 2020;119:365-84.
7. Gallo S, Galvis Franco W, Jaramillo Ayerbe F, Van den Enden L. Leishmaniasis cutánea crónica en el nuevo mundo: serie de casos de otra gran simuladora. Rev Asoc Colomb Dermatol. 2022;30:138-47.
8. Handler MZ, Patel PA, Kapila R, Al-Qubati Y, Schwartz RA. Cutaneous and mucocutaneous leishmaniasis: differential diagnosis, diagnosis, histopathology, and management. J Am Acad Dermatol. 2015;73:911-26, 927-8.
9. Aronson NE, Joya CA. Cutaneous leishmaniasis: updates in diagnosis and management. Infect Dis Clin North Am. 2019;33:101-17.

Medicina CUTÁNEA Ibero-Latino-Americana

PERMANYER

Check for updates

CASE REPORT

Treatment of scleromyxedema with low doses of intravenous immunoglobulin: report of a case

Tratamiento del escleromixedema con dosis bajas de inmunoglobulina intravenosa: reporte de un caso

Lucía M. Córdoba, Mercedes Costantino-Zanchin, Virginia D. Dimotta, Dolly A. Lucini, María C. Mancinelli, and María A. Verea*

Servicio de Dermatología, Hospital Interzonal Especializado en Agudos y Crónicos San Juan de Dios de La Plata, La Plata, Argentina

Abstract

Scleromyxedema is a rare disease with a chronic course and unknown etiopathogenesis. It is characterized by dermal mucin deposits, fibrosis, and proliferation of fibroblasts in the dermis. Clinically, it manifests with an eruption of waxy papules and induration of the skin. It can be accompanied by systemic involvement and be associated with other diseases. Its treatment is not standardized and is currently based on case reports. We present the clinical case of a patient with scleromyxedema who received treatment with intravenous immunoglobulin in doses lower than those recommended in the literature associated with systemic corticotherapy with a good response.

Keywords: *Cutaneous mucinosis. Scleromyxedema. Intravenous immunoglobulin.*

Resumen

El scleromyxedema es una enfermedad rara, de curso crónico y etiopatogenia desconocida. Se caracteriza por presentar depósitos de mucina dérmicos, fibrosis y proliferación de fibroblastos en la dermis. Clínicamente se expresa con erupción de pápulas céreas e induración de la piel. Puede acompañarse de compromiso sistémico o asociarse con otras enfermedades. Su tratamiento no está estandarizado y se basa actualmente en reportes de casos. Presentamos el caso clínico de un paciente con scleromyxedema que recibió tratamiento con inmunoglobulina intravenosa en dosis menores que las recomendadas en la literatura, asociado a corticoterapia sistémica, con buena respuesta.

Palabras clave: *Mucinosis cutánea. Scleromyxedema. Inmunoglobulina intravenosa.*

***Correspondence:**
Virginia D. Dimotta
E-mail: virginiadimotta@gmail.com

Date of reception: 02-05-2023
Date of acceptance: 02-11-2023
DOI: 10.24875/MCUTE.M24000007

Available online: 26-04-2024
Med Cutan Iber Lat Am. (Eng). 2024;52(1):28-33
www.MedicinaCutaneaILA.com

Introduction

Scleromyxedema is a rare, underdiagnosed condition that usually affects adults between 30 and 80 years old, with no predominance of race or sex, and its etiopathogenesis is unknown[1]. Clinically, it manifests with the appearance of numerous hard and waxy papules in a symmetric and generalized pattern, along with skin sclerosis. In most cases, it presents with a monoclonal gammopathy and associated severe systemic disorders[1-3].

Diagnosis is based on the recognition of clinical and histopathological findings and the presence of paraproteins or the absence of thyroid disorder in the lab test results[3].

The most widely used first-line therapy is IV immunoglobulin (IVIG), for its safety and efficacy profile[4,5]. Thalidomide and systemic glucocorticoids are considered second-line therapies and are administered alone or in combination with IVIG[4,6].

We present the case of a patient diagnosed with scleromyxedema treated with IVIG (0.5 g/kg), with a good response.

Case report

A 57-year-old male with a personal history of hypertension, benign prostatic hyperplasia, and placement in 2017 of a ventriculoperitoneal shunt valve due to cerebral arteriovenous malformation, was referred to our service by neurosurgery due to 1-year history generalized skin thickening signs.

On physical examination, he presented skin with a tense appearance with a marked increase in consistency and a decrease in elasticity. On the face, ear, neck, extension surface of the forearms, wrists, and dorsum of both hands, a symmetric eruption of millimetric, waxy papules, distributed linearly, along with sclerodactyly and a central depression surrounded by the raised edge in the interphalangeal joints ("doughnut sign") was observed (Fig. 1). On the face, the patient exhibited a leonine appearance with marked folds in the glabellar area, sparing eyebrows and eyelashes (Fig. 2), and on the abdomen, back, and upper and lower limbs, accentuation of furrows with redundant skin folds ("shar pei sign") (Fig. 3).

The clinical picture conditioned oral and ocular opening and joint mobility. Concomitantly, the patient showed general discomfort, dysphagia, and significant weight loss in recent months.

With a suspected diagnosis of scleromyxedema, a skin biopsy was taken for histopathological examination, which reported abundant dense collagen connective tissue, deposits of perivascular and perianexial mucoid material, and positive alcian blue staining (Fig. 4).

Systemic involvement was evaluated in search for other associated conditions, in a multidisciplinary manner. As positive data, the electrophoretic proteinogram showed a slight increase in alpha-2 macroglobulin with a homogeneous band in the gamma zone, corresponding

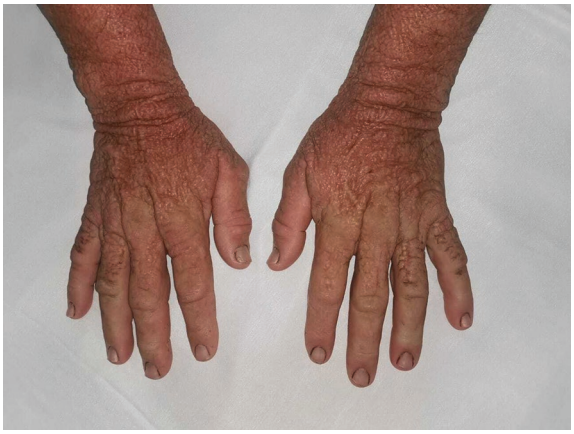


Figure 1. Eruption of waxy millimeter-sized papules on the dorsum of the interphalangeal joints, with the "doughnut sign".

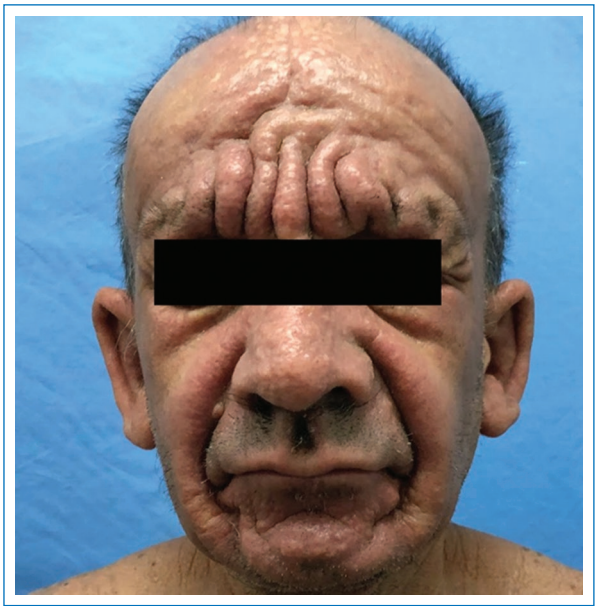


Figure 2. Eruption of firm, waxy papules, 2-3 mm in diameter; the glabella especially involved, with deep longitudinal furrows determining revealing typical leonine traits.

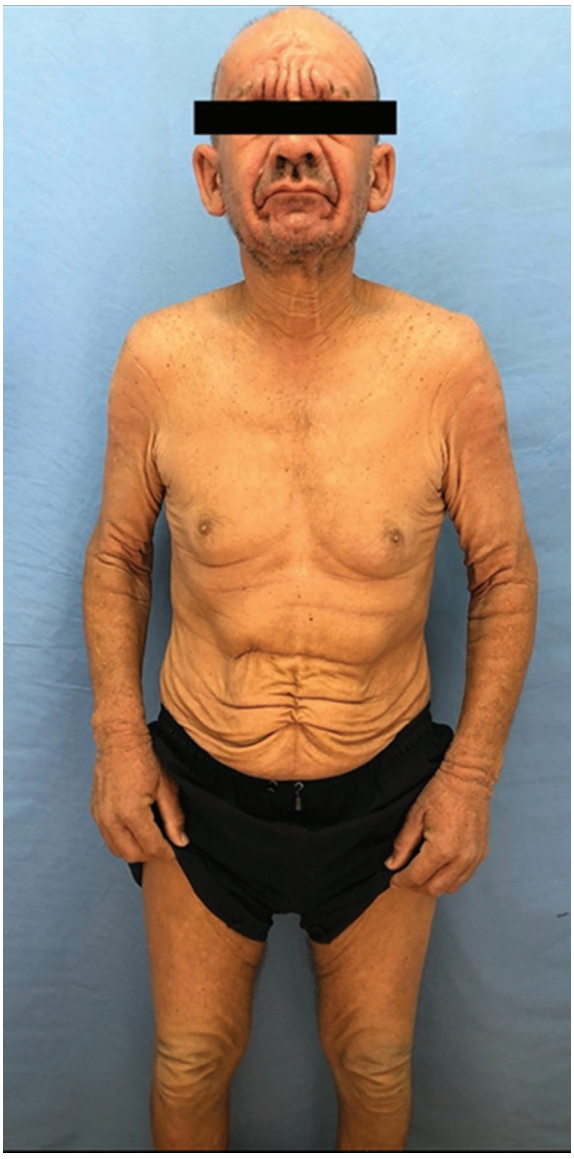


Figure 3. Thickening of the skin of the forehead; typically evident deep grooves with folds of redundant skin on abdomen and limbs.

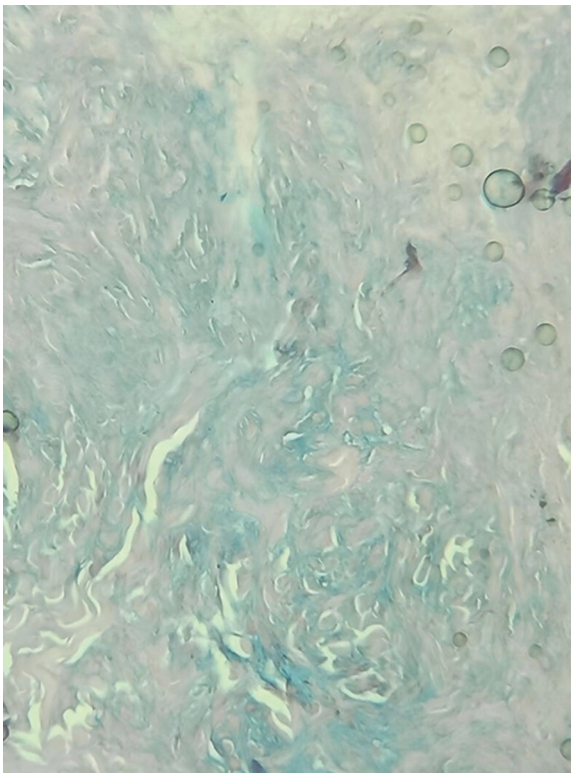


Figure 4. Histopathology. Positive alcian blue staining for acidic mucopolysaccharides. 10x.

to the G kappa monoclonal component, while the remaining immunoglobulins decreased. The blood test of peripheral blood and bone marrow aspiration was uneventful, which was consistent with the monoclonal gammopathy of clinical significance. Therefore, the hematology service decided to adopt an expectant approach with follow-up with an electrophoretic proteinogram every 3 months.

Thus, the diagnosis of scleromyxedema was confirmed. Due to difficulty in immediate access to IVIG, treatment was initiated with prednisone 0.5 mg/kg/day until the drugs became available. Within the first 3 months of IVIG, due to unavailability, doses of 0.5 g/kg/month were used, which were lower than those recommended in most literature reports (2 g/kg/month), with a good response (Fig. 5). After the first cycle of IVIG, the patient showed a notable improvement in general condition, with less infiltration of the skin, increased joint mobility, and oral opening, so it was decided to gradually reduce systemic corticosteroid therapy until its suspension.

Afterward, IVIG was increased up to 2 g/kg/month. The patient completed a total of nine cycles over 18 months due to the patient's irregular adherence, with favorable clinical evolution (Fig. 6).

Finally, the patient experienced neurological deterioration of ischemic origin (foci of gliosis in T2 and Flair sequences) due to complications of his underlying disease (cerebral arteriovenous malformation), with subsequent death.

Discussion

Cutaneous mucinoses are a heterogeneous group of conditions characterized by abnormal deposition of mucin in the dermis. They can be primary, where this is the main histopathological finding, or secondary,

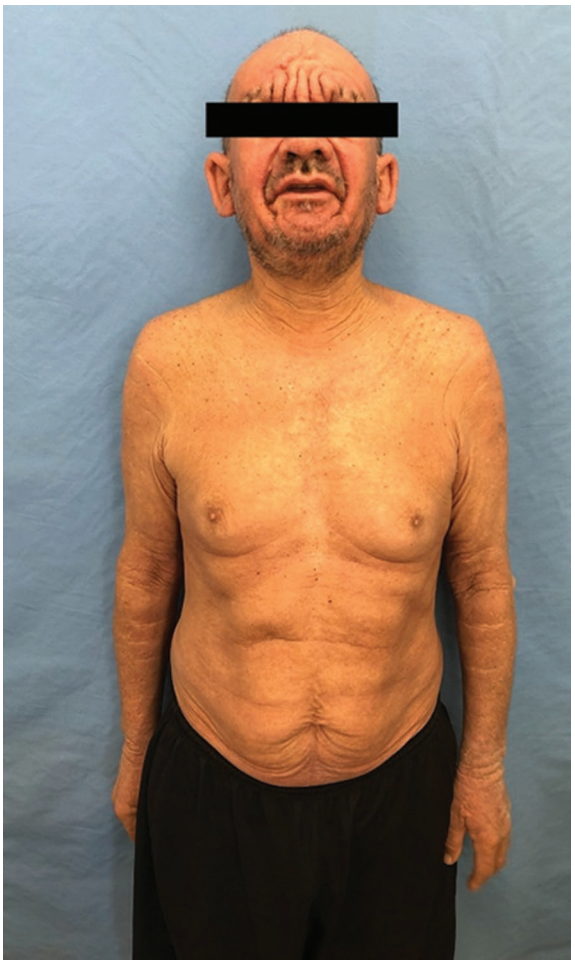


Figure 5. Improvement of the cutaneous condition after 3 months of treatment with low-dose IV immunoglobulin.

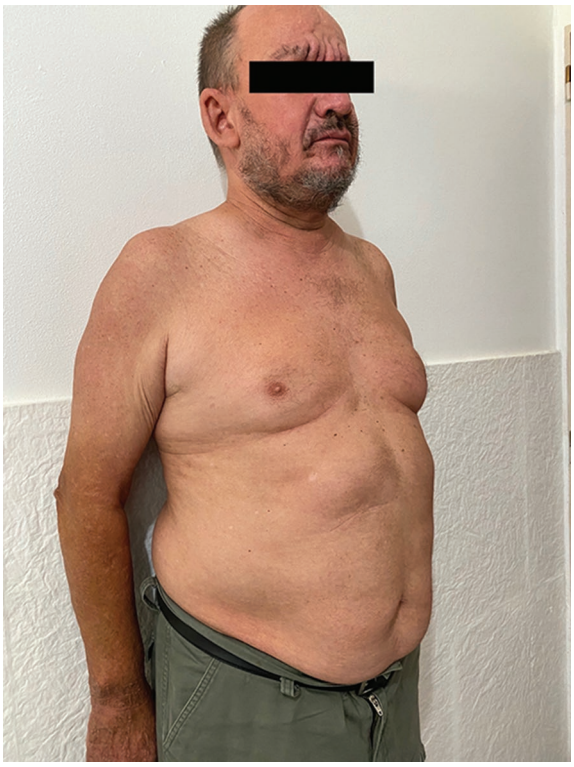


Figure 6. Cutaneous condition at 18 months of treatment with full dose IV immunoglobulin.

where its presence is an extra finding. The latter occurs in the context of other diseases and conditions such as lupus erythematosus, granuloma annulare, basal cell carcinoma, etc.). Primary mucinoses, in turn, can be degenerative/inflammatory (scleromyxedema) or hamartomatous/neoplastic[1].

Scleromyxedema is considered a subtype of lichen myxedematosus, which is classified into three clinicopathological subgroups: generalized papular and sclerodermoid, localized, and atypical[3,7]. The first references to this term are attributed to Dubreuilh in 1906 and Reitman in 1908, and its division to the review conducted by Montgomery and Underwood was performed in 1953. It was Gottron who, in 1954, first coined the term "scleromyxedema" for the generalized and sclerotic form[3].

Its pathogenesis is unknown, but the main hypothesis is that cytokines (such as interleukin 1, tumor necrosis factor-alpha, and tumor growth factor beta) stimulate the synthesis of glycosaminoglycans and fibroblast proliferation in the skin[4].

Clinical remission of the dermatosis, along with a reduction in protein M, following autologous hematopoietic stem cell transplantation, points to bone marrow and secondary lymphoid organs as the source of the circulating profibrogenic factors involved[8,9].

Clinically, it is characterized by the presence of 2 mm to 3 mm in size firm, symmetric, and generalized papules, waxy, with linear arrangement and marked skin induration, and is most commonly found on the face, neck, hands, forearms, upper trunk, and thighs. Itching may be present. Mucous membranes and the scalp are spared. In the glabella, deep longitudinal furrows with thickening of the skin, which may present erythema and edema (leonine facies), can typically be observed. Similar changes can be seen on the trunk and limbs ("shar pei sign")[10].

As the condition progresses, erythematous and infiltrated plaques with skin stiffness, sclerodactyly, and decreased mouth and joint mobility may appear. Characteristically, on the dorsum of the hands, at the proximal interphalangeal joints, central depressions

with raised edges ("doughnut sign") can be observed. Painless nodules may be present in the subcutaneous tissue. Telangiectasias and calcinosis are always absent, unlike what occurs in systemic sclerosis[10,11].

It typically has an unpredictable, chronic, and progressive course. A total of 77% of patients may present extracutaneous signs, with neurological (30%), rheumatological (25%), and cardiac (22%) signs being the most common of all[12].

It can affect the peripheral and central nervous system. Dermatoneuro syndrome has been described in < 10% of patients, characterized by a flu-like prodrome, followed by high fever, seizures, and coma. Usual diagnostic tests used to evaluate these findings often test negative[12]. The mechanism involved is unknown to this date[13].

From a rheumatological point of view, it is characterized by the presence of arthralgia or arthritis of peripheral joints, especially the hands[14]. Cardiac involvement is due to congestive heart failure, ischemia, arrhythmia, or pericardial effusion[12].

The role of monoclonal gammopathy is still under discussion. Although most patients present with blood dyscrasia, paraprotein concentrations do not correlate with the severity of the disease, progression, or treatment response. This is usually IgG with lambda/kappa light chains (83.2%), with progression to multiple myeloma in 10% of cases[10,15].

In addition, dysphagia and esophageal dysmotility[15], respiratory involvement with exertional dyspnea[12], acute renal failure[14], and ocular signs such as corneal opacities and ectropion have been reported[12,15].

Pathologically, two patterns are evident: the classic type (with the microscopic triad of mucin deposition in the reticular dermis, increased collagen, and irregularly arranged fibroblast proliferation) and a pattern similar to interstitial granuloma annulare that has been recently described[16]. Dermic mucinoses are confirmed by special stains of alcian blue and colloidal iron[11,17].

The diagnosis is based on the recognition of the following four clinicopathological criteria: (1) generalized, papular, and sclerodermoid eruption; (2) microscopic triad; (3) monoclonal gammopathy; and (4) absence of thyroid disorder.

Atypical forms include cutaneous involvement in the absence of monoclonal gammopathy or an interstitial granulomatous pattern in the histopathology examination[3].

Treatment is often systemic. Consideration of comorbidity, disease distribution, clinical experience, and accessibility are essential.

High doses of IVIG, 2 g/kg distributed over 2-5 days every 4 weeks, are suggested as first-line therapy (level of evidence 2C)[4-6]. Symptom improvement is usually evident after the first or second cycle, with high rates of rheumatological and neurological response[4,8]. Intervals can be extended up to 6 weeks based on clinical progression. Long-term maintenance treatment is usually required[6,14,18], as the rates of recurrence are high once administration has been suspended.

Lower dose protocols (0.4-0.5 g/kg/month) have been described effectively in patients with limited disease[8,19].

The mechanism of action is still unclear, although a decrease in circulating interleukin 17-producing CD8-positive cells and a reduction in gene expression of tumor growth factor-beta and various interferon-induced proteins have been detected in affected tissue[20].

If monotherapy with IVIG fails, or in the presence of contraindications, thalidomide and systemic corticosteroids are considered second-line therapeutic options.

A successful combination of IVIG plus thalidomide[7,18] at doses of 50-100 mg to 150-400 mg has been reported.

Corticosteroid therapy at a dose of 0.5-1 mg/kg/day of prednisone is associated with improvement in cutaneous and systemic signs and paraproteinemia. This could be due to its immunosuppressive and anti-fibroblast effects. If no therapeutic effect has been achieved after 6 weeks, consideration should be given to switching to a different regimen[4,8,14].

Patients with severe or refractory disease may benefit from interventions aimed at treating associated plasma cell dyscrasia, such as bortezomib with dexamethasone, melphalan, and autologous stem cell transplantation[8,14]. Complete remission was reported following treatment with the latter back in 2001.

Other treatments described in the literature include PUVA, UVA1, systemic retinoids, cyclosporine, electron beam radiation, plasmapheresis, and extracorporeal photochemotherapy, with variable results[8,14].

Conclusions

The publication of this case aims to show a rare, chronic, and disabling condition, the etiopathogenesis of which is unknown and lacks randomized clinical trials to support definitive specific treatment.

Regarding treatment, our patient showed a good response to low-dose IVIG within the first 3 months (with few reports in the literature)[8,19], and thereafter continued intermittently at full dose for 18 months with favorable evolution.

We emphasize the role of the dermatologist in the initial evaluation of this disease and the multidisciplinary approach for the early detection of associated systemic involvement.

Funding

The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Rongioletti F, Merlo G, Cinotti E, Fausti V, Cozzani E, Cribier B, et al. Scleromyxedema: a multicenter study of characteristics, comorbidities, course, and therapy in 30 patients. J Am Acad Dermatol. 2013;69:66-72.
2. Medina Castillo DE, Martínez Muñoz JA, Caballero Hernández N, Ortiz Guerrero RM, Ortiz Valdés CP, Rodríguez Barón CB et al. Escleromixedema. Dermatol Rev Mex. 2016;60:24-36.
3. Rongioletti F. Lichen myxedematosus (papular mucinosis): new concepts and perspectives for an old disease. Semin Cutan Med Surg. 2006;25:100-4.
4. Hoffmann J, Enk A. Scleromyxedema. J Dtsch Dermatol Ges. 2020;18:1449-67.
5. Sillard L, Passeron T, Cardot Leccia N, Perrin C, Lacour J, Ortonne J. Efficacy of intravenous immunoglobulin in the treatment of scleromyxoedema. Ann Dermatol Venereol. 2010;137:48-52.
6. Enk A, Hadaschik E, Eming R, Fierlbeck G, French L, Girolomoni G, et al. European Guidelines (S1) on the use of high-dose intravenous immunoglobulin in dermatology. J Dtsch Dermatol Ges. 2017;15:228-41.
7. Wong R, Chia J, Haber R. Review of primary cutaneous mucinoses in non-lupus connective tissue diseases. J Cutan Med Surg. 2018;22:65-70.
8. Haber R, Bachour J. Scleromyxedema treatment: a systematic review and update. Int J Dermatol. 2020;59:1191-201.
9. Lacy M, Hogan WJ, Gertz MA, Dispenzieri A, Rajkumar V, Hayman S, et al. Successful treatment of scleromyxedema with autologous peripheral blood stem cell transplantation. Arch Dermatol. 2005;141:1277-82.
10. Rongioletti F, Rebora A. Updated classification of papular mucinosis, lichen myxedematosus, and scleromyxedema. J Am Acad Dermatol. 2001;44:273-81.
11. Gómez Díez S, Maldonado C, López Escobar M, Manjón JA, Jalón A, Rodríguez Vigil T, et al. Escleromixedema. Actas Dermosifiliogr. 2003;94:627-30.
12. Pomann J, Rudner E. Scleromyxedema revisited. Int J Dermatol. 2003;42:31-5.
13. Bielsa I, Benvenutti F, Guinovart RM, Ferrándiz C. Escleromixedema y síndrome dermato-neuro: buena respuesta al tratamiento con glucocorticoides e inmunoglobulinas endovenosas. Actas Dermosifiliogr. 2012;103:317-20.
14. Knobler R, Moinzadeh P, Hunzelmann N, Kreuter A, Cozzio A, Mouthon L, et al. European dermatology forum S1-guideline on the diagnosis and treatment of sclerosing diseases of the skin. Part 2: Scleromyxedema, scleredema and nephrogenic systemic fibrosis. J Eur Acad Dermatol Venereol. 2017;31:1581-94.
15. Neufeld M, Sunderkötter C, Moritz K. Skleromyxödem. Hautarzt. 2018;69:916-21.
16. Rongioletti F, Cozzani E, Parodi A. Scleromyxedema with an interstitial granulomatous-like pattern: a rare histologic variant mimicking granuloma annulare. J Cutan Pathol. 2010;37:1084-7.
17. Efthimiou P, Blanco M. Intravenous gammaglobulin and thalidomide may be an effective therapeutic combination in refractory scleromyxedema: case report and discussion of the literature. Semin Arthritis Rheum. 2008;38:188-94.
18. Blum M, Wigley FM, Hummers LK. Scleromyxedema: a case series highlighting long-term outcomes of treatment with intravenous immunoglobulin (IVIG). Medicine (Baltimore). 2008;87:10-20.
19. Körber A, Franckson T, Grabbe S, Dissemond J. Successful therapy of scleromyxoedema Arndt-Gottron with low-dose intravenous immunoglobulin. J Eur Acad Dermatol Venereol. 2007;21:553-4.
20. Mecoli C, Conover T, Fava A, Cheadle C, Boin F, Wigley F, et al. Clinical and molecular phenotyping in scleromyxedema pretreatment and posttreatment with intravenous immunoglobulin. Arthritis Care Res (Hoboken). 2020;72:761-7.

Medicina CUTÁNEA Ibero-Latino-Americana

PERMANYER

Check for updates

CASE REPORT

Secondary ear involvement as a reaction to the use of cytarabine in a patient diagnosed with acute myeloid leukemia

Compromiso de pabellones auriculares secundario al uso de citarabina en paciente con leucemia mieloide aguda

Valeria Arciniegas-Grisales[1,2], Paola A. Rueda-Galvis[1,2], Valentina Rodelo-Sánchez[1], Laura T. Osorio-Moreno[1], Ana M. Mejía-Giraldo[1,2,3], and Jorge A. Bermúdez-Montero[4]*

[1]Facultad de Ciencias de la Salud, Universidad CES; [2]Servicio de Dermatología, Universidad CES; [3]Servicio de Dermatología, Hospital General de Medellín Luz Castro de Gutiérrez; [4]Servicio de Medicina Interna, Hospital General de Medellín Luz Castro de Gutiérrez. Medellín, Antioquia, Colombia

Abstract

Cytarabine or Ara-C is one of the most widely used antineoplastic drugs in the treatment of rapidly growing hematologic malignancies. Its use has been associated with multiple systemic and cutaneous side effects. Among the main dermatological reactions, morbilliform rash and acral erythema stand out. The latter has an infrequent presentation commonly known as "cytarabine ears." We present the case of a patient diagnosed with acute myeloid leukemia, who developed a dermatosis with isolated involvement of the ears during the 8th day after starting cytarabine.

Keywords: *Acute myeloid leukemia. Cytarabine. Ears. Drug eruptions.*

Resumen

La citarabina o Ara-C es uno de los medicamentos antineoplásicos más usados en el tratamiento de las neoplasias hematológicas de rápido crecimiento. El uso de este fármaco se ha asociado a múltiples efectos adversos sistémicos y cutáneos. Dentro de las principales reacciones dermatológicas destacan el exantema morbiliforme y el eritema acral. Este último tiene presentaciones poco frecuentes, como las «orejas de citarabina». Se describe el caso de una paciente con diagnóstico de leucemia mieloide aguda, quien al octavo día de iniciar citarabina presentó una dermatosis limitada a los pabellones auriculares.

Palabras clave: *Leucemia mieloide aguda. Citarabina. Orejas. Farmacodermia.*

Correspondence:
Valeria Arciniegas-Grisales
E-mail: valeria.arciniegas5@gmail.com

Date of reception: 11-11-2022
Date of acceptance: 27-12-2023
DOI: 10.24875/MCUTE.M24000005

Available online: 26-04-2024
Med Cutan Iber Lat Am. (Eng). 2024;52(1):34-38
www.MedicinaCutaneaILA.com

Introduction

Cytarabine is a pyrimidine analog used for over 40 years to treat various hematologic malignancies, such as acute myeloid leukemia, acute lymphoblastic leukemia, and non-Hodgkin lymphoma[1]. High-dose cytarabine formulation has shown excellent results in increasing long-term survival; however, numerous studies have documented that the known side effects of this drug are dose-dependent[2]. Among these adverse events are bone marrow suppression, fever, cerebellar toxicity, cardiomyopathy, hepatic and renal failure, necrotizing enterocolitis, pancreatitis, acute respiratory distress, corneal toxicity, and dermatologic signs, the latter occurring in approximately 53% of patients[3,4]. Dermatologic side effects may appear immediately or approximately 6 days after the start of therapy, as a delayed hypersensitivity reaction, largely attributed to cytokine release[5]. The most common cutaneous signs are generalized morbilliform rash and acral erythema, also known as palmar-plantar erythrodysesthesia. In addition, other reactions described, but rarely observed, include vasculitis, eccrine squamous syringometaplasia, and eccrine neutrophilic hidradenitis[2].

Specifically, palmar-plantar erythrodysesthesia presents as painful erythema with a predilection for acral sites such as the hands and feet but can even affect peripheral sites such as the ears referred to as "cytarabine ears"[6].

Case report

A 58-year-old woman with a past medical history of hypothyroidism and a diagnosis of acute myeloid leukemia with negative molecular study for the FLT3 gene, which encodes a tyrosine kinase receptor involved in hematopoiesis control, was admitted to our center for initiation of induction chemotherapy, protocol 7 + 3 with cytarabine (100 mg/m^2/dose for 7 days) and idarubicin (12 mg/m^2/dose from day 1 to 3). On the 4th day of treatment, she developed painful and pruritic lesions on both ears associated with fever. Physical examination revealed the presence of violaceous, scaly, edematous, infiltrated plaques, with well-demarcated regular borders in the bilateral retroauricular region (Fig. 1) without involvement of other areas. Initially, due to fever, the febrile neutropenia protocol was activated, and a broad-spectrum antibiotic regimen including vancomycin and cefepime was indicated.

Afterward, she was evaluated by the dermatology service, where treatment with 0.05% betamethasone cream every 12 h for 7 days and 50 mg diphenhydramine every 12 h for 7 days was initiated, resulting in the resolution of the lesions. During follow-up, she experienced prolonged induced aplasia, without response to granulocyte colony-stimulating factor, and a new bone marrow aspiration performed revealed persistence of the disease, leading to administration of second-line therapy with HAM protocol consisting of cytarabine 500 mg every 12 h on days 1, 2, 3, and 4, mitoxantrone 20 mg on days 3, 4, and 5, and filgrastim 300 mg from day 6 until neutropenia recovery. After starting cytarabine infusion, the patient developed lesions in the bilateral retroauricular region once again, with less involvement than the previous outbreak (Fig. 2). Topical management included a 1-week course of 0.05% betamethasone once a day plus a repairing cream with thermal water, zinc oxide, magnesium sulfate, and zinc sulfate, resulting in lesion remission.

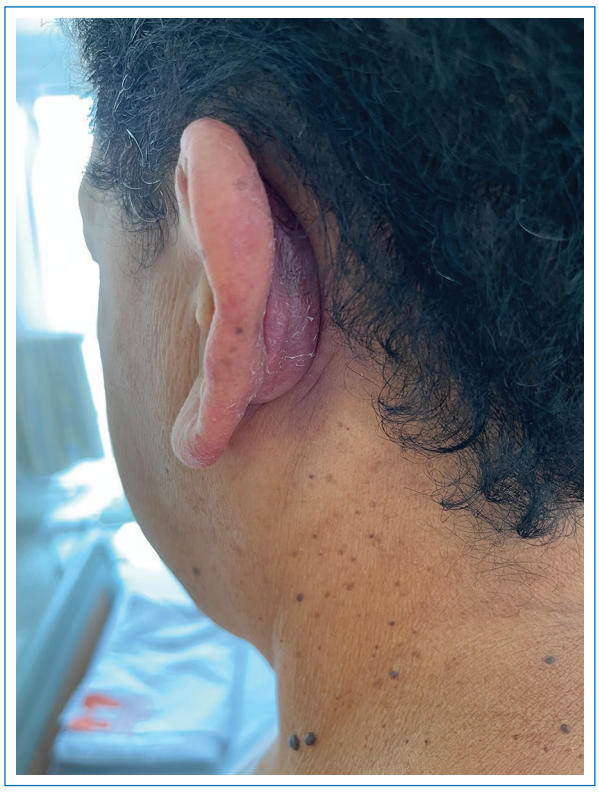


Figure 1. Scaly, edematous, infiltrated, well-demarcated, violaceous erythematous plaque with regular borders in the left retroauricular region.

Discussion

Cytarabine or cytosine arabinoside (Ara-C) is a synthetic pyrimidine antagonist and cytidine nucleoside analog, which acts by inhibiting the S phase of the cell cycle during DNA synthesis, thereby exerting an

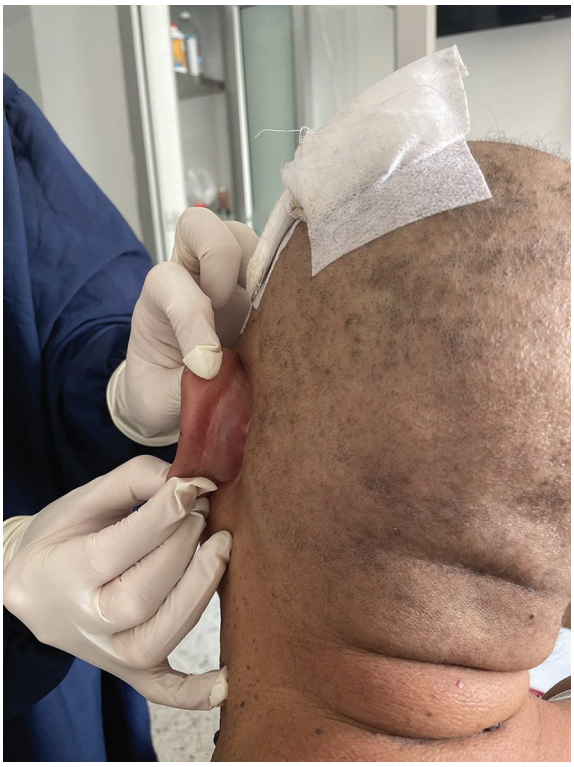


Figure 2. Slightly infiltrated, well-demarcated, violaceous erythematous plaque in the bilateral retroauricular region.

antineoplastic effect useful to treat hematologic neoplasms[7]. This drug is used in oncology, both in the induction (combined with anthracyclines) and in the consolidation phases. Usually, at high doses, numerous adverse events have been reported, such as severe myelosuppression and toxicity to various organs (GI, hepatic, central nervous system, ocular, or cutaneous, among others)[8,9].

Cutaneous toxicity has been described in the literature as a rare secondary manifestation of high doses, with an incidence ranging from 2% up to 72%[2,3,8]. The exact cause of this reaction is still unknown, but several hypotheses have been proposed to explain cytarabine toxicity to the skin:

– Delayed hypersensitivity reaction, with the appearance of lesions 1-2 weeks after drug exposure
– Vascular damage, primarily based on findings of acral erythema, which is the most common cutaneous adverse event
– Direct epithelial damage and accumulation of toxicity associated with cytarabine excretion by the eccrine glands[2,6].

Hence far, no specific risk factors associated with the presentation of cutaneous reactions to cytarabine have been described, such as age, history of atopy, previous drug reactions, type of acute myeloid leukemia, or chemotherapy regimen[7]. High doses of cytarabine seem to be related to these reactions, but dermatologic signs can even occur with low doses, as in our case[10].

Cytarabine can cause various types of skin reactions, which will be described in detail below. The typical cytarabine-induced skin rash develops between 6 and 12 h after starting the drug and resolves with therapy cessation[8]. This reaction can manifest as a maculopapular rash, morbilliform rash, or hand-foot syndrome with the involvement of palms and soles. In the latter, acral erythema is observed and is associated with pain, tingling sensation, and paresthesias; even the trunk and limbs can be compromised too. Isolated ear involvement has also been reported, for which the term "cytarabine ears" is used, being one of the less common presentations of acral erythema, with only nine reported cases reported to this date[3,11].

In these cases, a biopsy of the affected tissue shows vacuolar degeneration of basal cells and dermal neutrophilic infiltrate[3]. However, histopathology is not necessary to diagnose this reaction as it is a benign and self-limiting condition that resolves with drug cessation, within 15-30 days, without scarring or with only mild post-inflammatory hyperpigmentation[7].

Among the differential diagnoses of "cytarabine ears" are drug eruptions, neutrophilic dermatoses such as sweet syndrome, contact dermatitis, graft-versus-host disease, vasculitis, skin infections, and leukemia cutis[2].

In some cases, symptomatic discomforts have been reported such as pain, tingling, or paresthesias. In these cases, topical and even systemic therapy with steroids as first-line therapy may be necessary[12]. In our case, management included oral antihistamines and topical steroids, with partial improvement.

On the other hand, Doval et al.[3] describe that only 27% of patients who presented with cutaneous lesions after the induction of chemotherapy with cytarabine had a recurrence of lesions in subsequent exposures, i.e., in the consolidation stage. The patient presented in this case report showed lesion recurrence after cytarabine administration in the second cycle of chemotherapy. In the second episode, the patient had less pronounced symptoms, therefore it was deemed unnecessary to discontinue the medication, and topical treatment with 0.05% betamethasone cream was continued, resulting in complete symptom resolution.

Table 1. Clinical and demographic characteristics of patients with acute myeloid leukemia on cytarabine who developed "cytarabine ears" cutaneous reactions associated with the initiation of drug use

Author (year)	Age/Sex	Day of "cytarabine ears" onset after starting cytarabine	Other skin signs	Febrile neutropenia	Biopsy	Treatment	Time to resolution of condition	Recurrence
Sahu et al.[10]	36 years/F	Day 4	No	No	No	Complete resolution at 14 days	Yes	
Prieto-Barrios et al.[4]	34 years/M	Day 6	No	Yes	Yes (superficial and deep neutrophilic dermatosis)	Corticosteroids (presentation and route of administration not described)	Not described	No
Jaruvijitrattana et al.[7]	53 years/F	Day 6	Multiple erythematous, pruritic, non-scaly papules and plaques on forehead, trunk, arms, and legs	No	Yes (superficial perivascular and perifollicular cellular infiltration, absence of peri-eccrine infiltration, basal membrane vacuolar alteration, scattered necrotic keratinocytes in epidermis. The inflammatory cell infiltration was mainly composed of lymphocytes, with few eosinophils and scattered necrotic keratinocytes)	Oral cetirizine 10 mg/12 h and 0.1% triamcinolone acetate cream every 12 h	Partial resolution at 10 days and complete in 1 month	No
Doval et al.[3]	41 years/F	Day 6	No	Yes	No	Partial resolution at 48 h and complete in 5 days	No	
Doval et al.[3]	60 years/F	Day 8	No	No	Oral fexofenadine	Complete resolution in 72 h	No	
Doval et al.[3]	42 years/F	Day 7	No	No	1% hydrocortisone cream plus oral analgesics	Partial resolution at 12 days and complete in 15 days	No	
Tamazian et al. (2021)[6]	15 months/M	Day 7	Symmetrical erythema on auricular shells, multiple erythematous papules on scalp, neck, trunk, and limbs	No	Yes (minimal chronic perivascular and perianexial inflammation with mild dermal edema)	Cytarabine suspension; 0.1% triamcinolone cream every 12 h	Partial resolution on 1 week; no report of complete resolution	Yes
Anesi et al.[5]	56 years/F	Day 8	No	No	Not described	Not described	Not described	

F: Female; M: Male.

Isolated ear involvement is rare, with very few documented cases in the literature. When reviewing the published cases to date of patients with "cytarabine ears" (Table 1), a predominance of female sex and a mean age of presentation of 53 years are evident, being these demographic characteristics similar to those of our patient.

Conclusions

We presented the case of a patient with acute myeloid leukemia who experienced a cytarabine-induced cutaneous adverse reaction involving the bilateral retroauricular region, known as "cytarabine ears." Due to the benign and self-limiting nature of this manifestation, it was deemed unnecessary to reduce the dose or discontinue the drug in patients with diseases limited to the skin. In addition, we should mention that a minority of patients experience a recurrence of the adverse cutaneous reaction after a new exposure, as was the case of our patient. Dermatologists and oncologists alike should be familiar with this adverse cutaneous reaction, thus avoiding unnecessary tests and invasive procedures.

Funding

The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval and informed consent

This work was reviewed and approved by the Research Committee of the Hospital General de Medellín - Luz Castro de Gutiérrez, Medellín, Colombia, following the principles of the Declaration of Helsinki and Resolution 8430/1993 of the Ministry of Health of Colombia.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Lichtman MA. A historical perspective on the development of the cytarabine (7 days) and daunorubicin (3 days) treatment regimen for acute myelogenous leukemia: 2013 the 40th anniversary of 7+3. Blood Cells Mol Dis. 2013;50:119-30.
2. Ruben BS, Yu WY, Liu F, Truong SV, Wang KC, Fox LP. Generalized benign cutaneous reaction to cytarabine. J Am Acad Dermatol. 2015;73:821-8.
3. Doval D, Kumar Sharma S, Kumar M, Khandelwal V, Choudhary D. Cytarabine ears — a side effect of cytarabine therapy. J Oncol Pharm Pract. 2020;26:471-3.
4. Prieto-Barrios M, Velasco-Tamariz V, Tous-Romero F, Burillo-Martinez S, Calleja-Algarra A, Aragón-Miguel R, et al. Ara-C ears: an actual drug-induced reaction or a distinctive manifestation of a neutrophilic dermatosis? JDDG J Dtsch Dermatol Ges. 2018;16:214-6.
5. Anesi GL, Levine D, Attar EC, Fathi AT. Bilateral ear swelling and erythema after chemotherapy: a case of Ara-C ears. J Clin Oncol. 2012;30:e146.
6. Tamazian S, Oboite M, Larijani M, Oliver B, Milbar H, Jen M, et al. Toxic erythema of chemotherapy affecting the ears of an infant: a case report. Pediatr Dermatol. 2021;38:512-3.
7. Jaruvijitrattana P, Chanprapaph K. Bilateral ear swelling and erythema after chemotherapy: a case report of Ara-C ears. Case Rep Dermatol. 2019;11:226-32.
8. Grille S, Guadagna R, Boada M, Irigoin V, Stevenazzi M, Guillermo C, et al. Citarabina y reacciones cutáneas en leucemia aguda mieloide. Med B Aires. 2013;73:535-8.
9. Krulder JWM, Vlasveld LT, Willemze R. Erythema and swelling of ears after treatment with cytarabine for leukemia. Eur J Cancer Clin Oncol. 1990;26:649-50.
10. Sahu KK, Yanamandra U, Malhotra P. Ara-C related red ear syndrome. Ear Nose Throat J. 2019;98:169-70.
11. Sanmartín O, Beato C, Suh-Oh HJ, Aragón I, España A, Majem M, et al. Manejo clínico de los eventos adversos cutáneos en pacientes tratados con quimioterapia: consenso nacional de la Academia Española de Dermatología y Venereología y de la Sociedad Española de Oncología Médica. Actas Dermo-Sifiliogr. 2019;110:448-59.
12. Bolognia JL, Cooper DL, Glusac EJ. Toxic erythema of chemotherapy: a useful clinical term. J Am Acad Dermatol. 2008;59:524-9.