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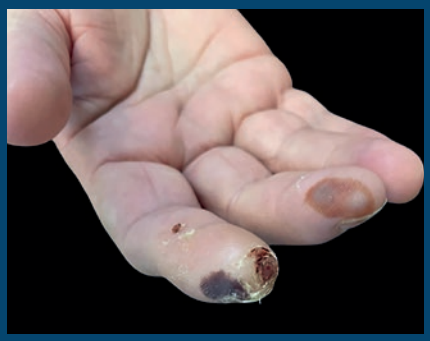

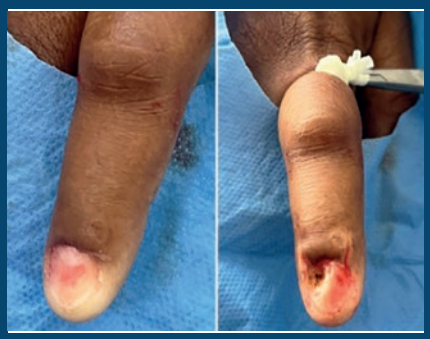

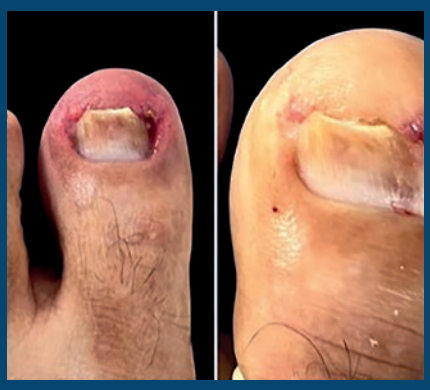

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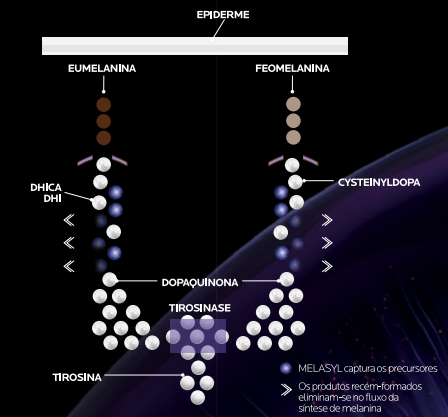

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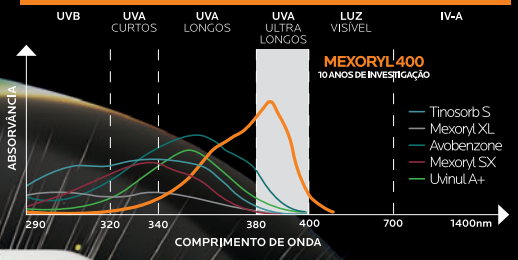

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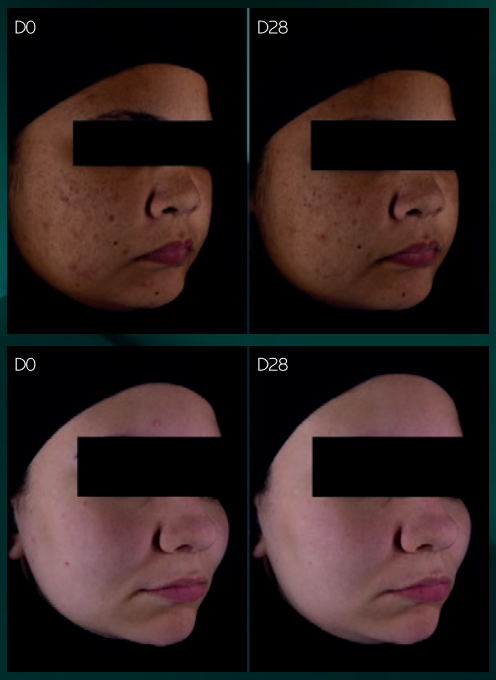

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3. Estudo clínico, 55 indivíduos, aplicação 2x/dia após 8 semanas. Contagem do nº de PIH persistentes por um dermatologista.
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REVIEW ARTICLE

Diagnosis of nail disorders: a literature review

Diagnóstico de afecções ungueais: uma revisão de literatura

Thairine H. Oliveira-Lima[1], Renata M. Oyama-Okajima[1,2], Silvia F. Rodrigues-Müller[1], Marília B. Xavier[1], Airton K. Motizuki[1], and Carla A. Avelar-Pires[1,2]*

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Abstract

The nail apparatus performs essential functions, such as protection and assistance in fine touch, making its integrity crucial for daily activities. The loss of its functionality can hinder routine tasks, directly impacting the quality of life. However, diagnosing nail disorders presents significant challenges due to the complexity of conditions affecting the nails and the overlap of features among different diseases. Diagnostic difficulty is further aggravated by professionals' lack of familiarity with techniques, such as dermoscopy, microscopy, microbial culture, and nail biopsy. In this study, we conducted a narrative literature review of articles indexed in PubMed from 2000 to 2024 that address the diagnosis of nail diseases. Selected studies were appraised according to methodological rigor and practical applicability, with an emphasis on the clinical relevance of their findings. Our review provides dermatologists and general practitioners with critical clinical insights that enhance understanding and management of patients with nail disorders.

***Keywords*:** Nail disorders. Differential diagnosis. Nail dermoscopy. Nail biopsy.

Resumo

O aparelho ungueal exerce funções essenciais, como proteção e auxílio no tato fino, sendo sua integridade fundamental para as atividades cotidianas. A perda de sua funcionalidade pode comprometer tarefas diárias, impactando diretamente a qualidade de vida. No entanto, o diagnóstico das afecções ungueais é um desafio devido à complexidade das condições que envolvem as unhas e à sobreposição de características entre as doenças. A dificuldade diagnóstica é agravada pela limitada familiaridade dos profissionais com técnicas como dermatoscopia, microscopia, estudos microbiológicos e biópsia ungueal. A metodologia do estudo envolveu uma revisão narrativa da literatura, com artigos publicados na plataforma PubMed entre 2000 e 2024, que abordam o diagnóstico de doenças ungueais e a análise dos artigos seguiu critérios de rigor metodológico e aplicabilidade prática, com foco na relevância clínica dos achados. Diante disso, essa revisão oferece insights clínicos importantes para a prática clínica de dermatologistas e médicos generalistas, auxiliando na melhor compreensão dos pacientes com patologias ungueais.

***Palavras-chave*:** Afecções ungueais. Diagnóstico diferencial. Dermatoscopia ungueal. Biópsia ungueal.

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Introduction

The nail apparatus performs essential functions for the organism, such as mechanical protection, assistance in fine tactile discrimination, object grasping, and contribute to the esthetics. Loss of nail integrity compromises various daily activities, directly affecting quality of life[1].

Diagnostic gaps in nail disorders in clinical practice are particularly attributable to insufficient familiarity with diagnostic methods, such as dermoscopy, dermatopathology of the nail, microbiological cultures, and, especially, nail biopsy. In dermoscopy, for example, nail signs are magnified and, together with physical examination, may enable diagnosis[2]. Proper use of this tool –as well as the others– requires thorough knowledge of nail anatomy, since the presentation of pathologic changes depends the affected area of the nail apparatus.

Among the nail diseases encountered in office practice, 50% are fungal, while the other 50% include neoplastic, inflammatory, traumatic, and systemic-related conditions[3]. The fungal nail disease, termed onychomycosis, employs direct microscopic examination (DME) as its primary diagnostic test, due to its low cost and the provision of immediate information that can be crucial for determining appropriate patient therapy[4].

Nail neoplasms include both malignant and benign tumors, which are often mistaken for onychomycosis or benign nail pigmentation[5]. Nail biopsy is critically important in this context, being at times both diagnostic and therapeutic. Its performance depends on understanding the surgical anatomy of the nail unit, proper anesthesia and hemostasis, and targeting an abnormality for which histopathology can yield a definitive diagnosis.

Indications and techniques for nail biopsy vary according to the site and type of pathology. Nail bed biopsies can be performed easily with minimal scarring and are most commonly used to diagnose tumors, infectious and inflammatory nail disorders[6]. The principal indication for nail biopsy is to establish or exclude the diagnosis of melanoma[6].

Diagnosing nail conditions can sometimes be a challenging task, not only because of the large number of cutaneous and systemic diseases involving the nails, but also due to their shared clinical features. Therefore, understanding the peculiarities of each pathology, as well as the anatomy and physiology of the nail apparatus, is essential for a more correct diagnosis and for delivering more targeted and effective treatment.

Anatomy and physiology of the nail

The nail unit is one of the principal skin appendages, functioning as a mechanical and sensory protective organ[7]. Nail anatomy comprises five components: the nail plate, commonly known as the nail; the matrix, which produces the nail plate and lies beneath the proximal nail fold, and can be visible on the thumbs and great toes through the nail plate as the lunula, the proximal, distal, and lateral nail folds; and the nail bed, which supports the nail plate. Beneath the nail bed lie connective tissue and the phalanx with its ligaments that attach the nail to the underlying joint structures[8].

The nail plate is a modified form of the stratum corneum and is curved along both the longitudinal and transverse axes. This curvature allows anchorage into the proximal and lateral nail folds, ensuring stability. The nail folds assist in securing the plate to the nail bed; when diminished, there is a tendency for onycholysis (nail detachment), and when thickened, pathological ingrowth may occur[9]. The proximal nail fold, together with the cuticle and the plate, protects the matrix from radiation and chemical irritants that could impair its function[10].

Maturation and differentiation of matrix keratinocytes proceed along a distally oriented, oblique axis. Thus, keratinization of distal matrix cells forms the ventral aspect of the nail plate, while keratinization of proximal matrix cells forms the dorsal aspect[11]. Nail plate abnormalities generally result from pathologies affecting the matrix or from space-occupying lesions beneath the nail fold[11].

Fingernail growth takes approximately 6 months to completely replace the nail plate, whereas toenail growth takes about 12 months[12]. Nail growth rate decreases with age and may be partially or fully halted by systemic diseases, trauma, or certain medications[12].

The objective of this study is to describe the main nail pathologies in terms of their clinical and etiological characteristics, as well as to establish objective criteria and the main diagnostic tools for recognizing these most prevalent nail conditions.

Methods

This study is a structured narrative literature review, guided by the principles of Preferred Reporting Items for Systematic Reviews and Meta-Analyses rather than by the full protocol of a systematic review, which employed the terms “nail diseases,” “nail disorders,” “diagnosis,” “nail neoplasm,” “melanonychia,” “pigmentation

disorders," "nail surgery" and "histopathology" in combination with the Boolean operators "and" and "or." Priority was given to articles addressing the diagnosis of nail conditions, including original articles, literature reviews, meta-analyses, guidelines and consensus statements, and case reports focusing on nail diseases diagnosed by clinical, dermatoscopic or histopathological methods. Inclusion criteria comprised articles published in the PubMed database between 2000 and 2024, in portuguese, spanish or english, and relevant to the research objectives. Exclusion criteria included studies without an available abstract, published outside the specified period, or not focused on the diagnosis of nail diseases.

Results

A total of 9526 articles were retrieved from PubMed for analysis. Of these, 3253 articles were excluded due to platform filtering based on language and publication period, and 6263 articles were excluded for not meeting the inclusion criteria or for not being related to the research objective (Fig. 1).

After exclusions, the remaining articles consisted of one prospective study and nine review articles, which were thoroughly analyzed for this research. In this regard, the article analyses adhered to criteria of methodological consistency, scientific evidence, and practical applicability, and were categorized by the type of nail condition addressed (inflammatory, neoplastic, infectious, traumatic), the diagnostic method utilized, and the clinical relevance of the findings (Table 1).

The selection of nail diseases was based on the clinical significance of the results and the volume of information available in each included article; two nail conditions were discussed within each category (Table 2).

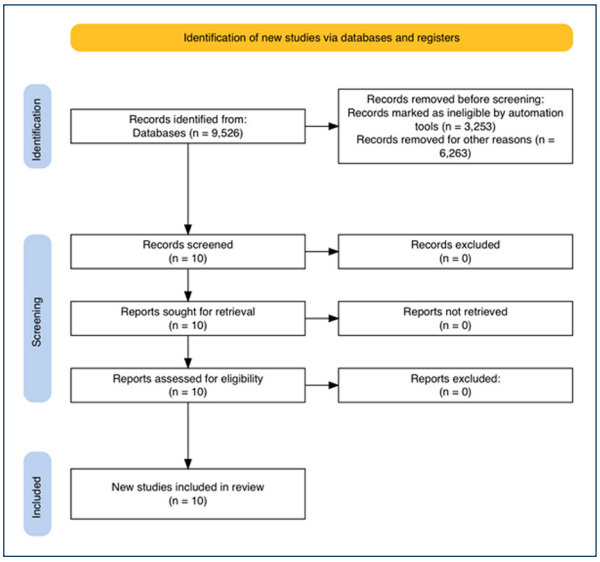

Figure 1. Flow diagram of the literature review according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Discussion

Inflammatory nail disorders

Nail psoriasis

The diagnosis of nail psoriasis can be based solely on cutaneous and/or osteoarticular signs and symptoms if a confirmed diagnosis of psoriasis vulgaris exists[13]. In the absence of these signs, diagnosis can be complex and must rely on complementary examinations. Hyperkeratosis, onychorrhexis, nail plate discoloration, and nail plate thickening generally resemble onychomycosis, which occurs in up to 60% of patients[13].

Nail unit involvement is characterized by pitting, rough and brittle nail plates, and pronounced transverse (Beau's) lines[14-16]. Signs of nail bed involvement include distal onycholysis with a proximal yellow-orange margin and serrated border, splinter hemorrhages, oil-drop (salmon) patch, subungual hyperkeratosis, and red or black hemorrhagic spots[14-16].

Nail pitting, distal onycholysis (separation of the nail plate from the underlying nail bed), oil-drop (salmon) patches, and splinter hemorrhages are key dermatoscopic features of nail psoriasis[16,17]. The formation of depressions, the characteristic nail pitting, is the most frequent finding and typically appears irregular on dermatoscopy, representing an indicative signal of nail psoriasis involvement (Fig. 2). This feature arises from parakeratosis of the nail matrix, leading to extrusion of parakeratotic cells as they emerge from beneath the proximal nail folds, thereby creating indentations on the nail surface[14-16].

The biopsy technique ideally indicated for the diagnosis of nail psoriasis is a punch biopsy without prior nail plate avulsion, as it preserves the morphology of the superficial tissue. However, it is difficult to introduce the punch through the nail plate while maintaining adhesion of the plate to the nail bed/matrix during instrument rotation without shear[18]. To reduce technical difficulty, the digit is soaked in warm water for a few minutes or the nail plate may be thinned by gentle abrasion[19]. Delay in performing the procedure and in specimen

Table 1. Articles selected for review

Title of article	Authors/year	Content	Category
"Optimal diagnosis and management of common nail disorders"	Lee and Lipner, 2022	Etiology, clinical presentation, diagnosis, and treatment of infectious and inflammatory nail diseases	Infectious, traumatic, and inflammatory
"Dermoscopy in the Evaluation of Nail Disorders"	Starace et al. 2021	Clinical presentation, diagnosis, and dermoscopy of nail lesions	Infectious, neoplastic, and traumatic
"Role of tangential biopsy in the diagnosis of nail psoriasis"	Bertanha et al. 2024	Clinical presentation and biopsy-based diagnosis of inflammatory nail diseases, such as nail psoriasis	Inflammatory
"Nail neoplasms"	Park et al. 2017	Clinical presentation, diagnosis, and histopathology of benign and malignant nail neoplasms	Neoplastic
"Nail Biopsy: A User's Manual"	Grover and Bansal, 2018	Techniques and types of nail biopsy for the diagnosis of nail diseases	Infectious and neoplastic
"Diagnosis and Management of Malignant Epithelial Nail Unit Tumors"	Iorizzo et al. 2024	Clinical presentation, diagnosis, dermoscopy, treatment, and prognosis of malignant epithelial tumors of the nail	Neoplastic
"Differential diagnosis of pigmented nail lesions"	Bertanha et al. 2024	Clinical presentation, dermoscopy, and diagnosis of pigmented nail disorders.	Infectious, neoplastic, and traumatic
"Histopathology of the nail unit"	Fernandez-Flores et al. 2014	Clinical presentation, histopathology, and diagnosis of nail unit diseases	Infectious, neoplastic, and inflammatory
"Nail surgery: General principles, fundamental techniques, and practical applications"	Queirós et al. 2022	Techniques and types of nail surgery for the treatment of nail lesions	Infectious, neoplastic, and traumatic
"Diagnosis of Melanonychia"	Starace et al. 2021	Clinical presentation, dermoscopy, histopathology, and diagnosis of pigmented nail disorders	Infectious and neoplastic

Table 2. Diagnostic tools to assist in each nail condition

Condition	Dermoscopy	Microscopy	Fungal culture	Nail biopsy
Nail psoriasis	X	-	-	X
Nail lichen planus	X	-	-	X
Onychomycosis	X	X	X	-
Paronychia	-	-	-	-
Glomus tumor	X	-	-	X
Onychopapilloma	X	-	-	X
Subungual melanoma	X	-	-	X
Squamous cell carcinoma	X	-	-	X
Onychocryptosis	-	-	-	-
Subungual hematoma	X	-	-	-

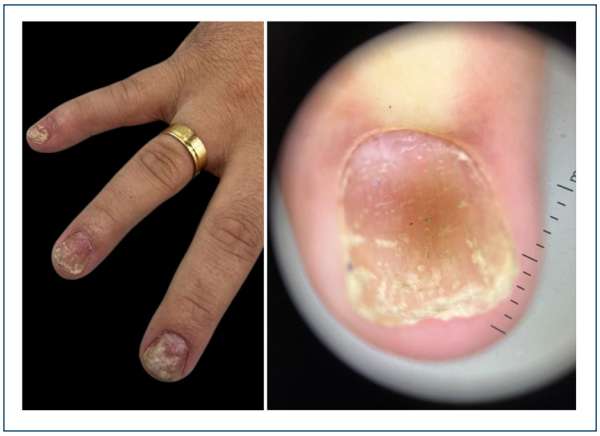

Figure 2. Clinical and dermoscopic image of nail psoriasis.

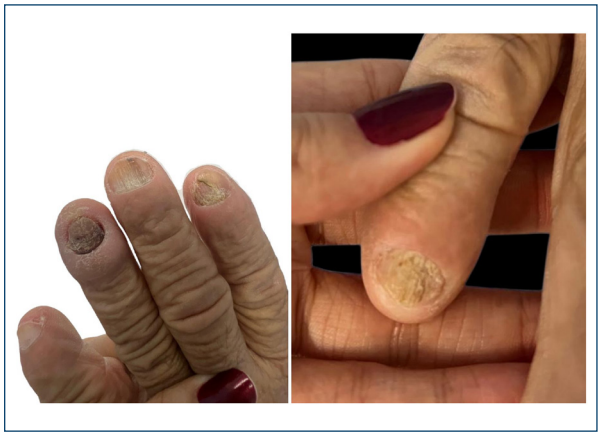

Figure 3. Nail lichen planus.

fixation can damage elements of the nail bed/matrix and compromise diagnostic accuracy[20].

In this regard, tangential excisional biopsy has gained prominence in the diagnosis of inflammatory nail diseases. In the tangential technique, the nail plate is carefully removed with a scalpel blade, preserving epithelial integrity and enabling artifact-free histopathological processing[18]. When bed and matrix alterations are present, a nail bed specimen is always preferable, both for technical ease and for a lower risk of scarring.

In a recent study by Bertanha *et al*. on tangential biopsy in nail psoriasis, good clinic-histopathological correlation was obtained using the following criteria: a mandatory criterion, dilated dermal papillary vessels, and at least three secondary criteria, namely, absence of spongiosis, presence of parakeratosis, psoriasiform epidermal hyperplasia, focal thinning of the granular layer and suprapapillary epidermis, and intra- or subcorneal neutrophilic exudate[18].

Nail lichen planus (LP)

Nail involvement occurs in 10% of patients with LP. Early recognition is crucial, as the disease can inflict extensive damage to the nail matrix, resulting in anonychia and proximal pterygium[21]. Clinical features of nail LP include brittle, roughened nail plates, a red or mottled lunula, onychorrhexis (vertical ridging of the nail plate), and longitudinal striations[22,23] (Fig. 3).

Onychoscopy may aid in detecting early LP changes[22,23]. Nail-bed involvement is manifested by plate fragmentation, chromonychia (discoloration of the nail plate or subungual tissue), splinter hemorrhages, onycholysis, subungual hyperkeratosis, and longitudinal grooves[22,23].

Twenty-nail dystrophy, or trachyonychia, is regarded as a variant of nail LP; its uniform appearance and the absence of proximal pterygium distinguish it from classic nail LP[21]. The idiopathic atrophic form presents acutely and typically progresses to diffuse nail destruction within a few months[21].

The diagnosis of nail LP requires biopsy with clinic-histopathological correlation. Key histopathological features include hyperkeratosis, hypergranulosis, a band-like inflammatory infiltrate, basal cell degeneration, and pigment incontinence[24]. In rare instances, subepidermal blister formation with prominent aggregates of colloid bodies may be observed, corresponding to the uncommon bullous variant of nail LP[24].

Infectious nail disorders

Onychomycosis

Onychomycosis is the most prevalent nail disease and can sometimes be confused with a variety of benign and malignant nail conditions[2,25]. This nail disorder represents all fungal infections of the nails and may involve the nail bed, plate, and matrix. It is the most prevalent nail disorder, affecting toenails more frequently than fingernails due to slower growth, reduced blood supply, and prolonged exposure to dark, humid environments[25,26].

Typical physical examination findings include hyperkeratosis of the nail bed, which often causes varying degrees of nail plate onycholysis[26]. A white or yellow discoloration of the nail plate is common, as well as subungual debris[26]. Trauma is a risk factor for onychomycosis, and violaceous/brown/black nail plate discoloration may also be present[26]. In longstanding or

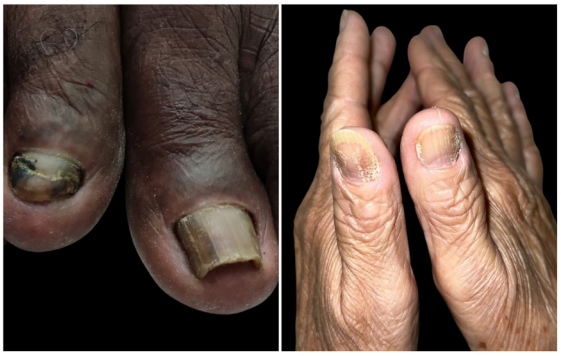

Figure 4. Onychomycosis involving finger nails.

severe cases, there may be extensive onychodystrophy with nail plate thickening, crumbling, ridging, onychocryptosis, and partial or complete nail loss[26] (Fig. 4). A dermatophytoma, or fungal abscesses, is a white/yellow or orange/brown longitudinal streak in the nail plate and is quite specific for onychomycosis[26].

Dermatoscopic features of onychomycosis include the "ruin appearance," "longitudinal streaks," and "spikes" at the proximal margin of the onycholytic area[27,28]. The "aurora borealis" sign (defined by the combination of multicolored chromonychia with longitudinal streaks, spikes, and onycholysis) demonstrates the highest sensitivity and specificity for this disorder[27,28]. The irregular, spiked proximal border corresponds to distal-to-proximal invasion of the nail bed's longitudinal ridges by dermatophytes[27,28].

Direct microscopy and fungal culture are the gold-standard methods for diagnosing onychomycosis[29]. Microscopic examination is performed after the nail is cleaned with 70% isopropyl alcohol, and then subungual debris samples are obtained, typically 8-10 fragments, to improve diagnostic accuracy. In a positive direct examination and fungal culture, hyphae, pseudohyphae, and spores are identified, confirming infection, although the specific organism is not identified in direct microscopy only in culture examination[25,29].

Nail biopsy is performed by obtaining a sample from the active site of infection, approximately 4 mm from the free edge[30]. After paraffin embedding, the material is stained with hematoxylin and eosin and special fungal stains, periodic acid-Schiff and methenamine silver, to visualize fungal structures under microscopy[30]. However, as with direct microscopic examination, histopathology should always be complemented by culture.

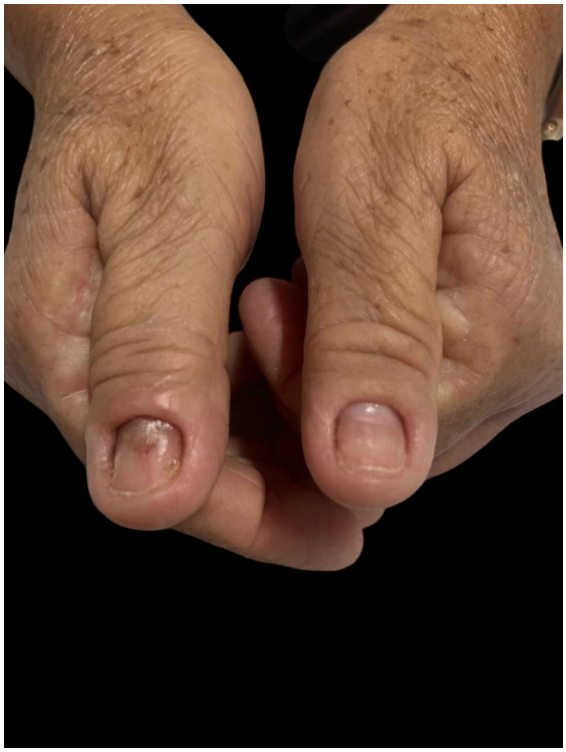

Figure 5. Paronychia involving both thumbs.

Paronychia

Paronychia is defined as inflammation or infection of the proximal or lateral nail folds[31,32]. Clinically, it presents with an acute onset of discomfort, tenderness, erythema, and edema. The acute form is characterized by disruption of the nail fold's protective barrier and pathogen invasion[31,32] (Fig. 5). Secondary infections often follow trauma, such as nail-biting or manipulation of ingrown nails, the latter being the most common etiologic factor[31].

If left untreated, infection may progress to the formation of granulation tissue around the nail fold and abscess development[31]. An untreated abscess in one fold can extend to involve all nail folds and may even spread into adjacent soft tissues of the affected digit[31,32]. Staphylococcus aureus is the primary pathogen, although *Streptococcus* spp., *Pseudomonas* spp., other Gram-negative bacteria, and *Candida albicans* can also invade the nail folds[31,32].

Diagnosis of paronychia is primarily clinical, based on patient history and physical examination, which helps differentiate it from other nail disorders[31-33]. For diagnostic confirmation, the digit-pressure test may be employed: when firm pressure over the affected fold

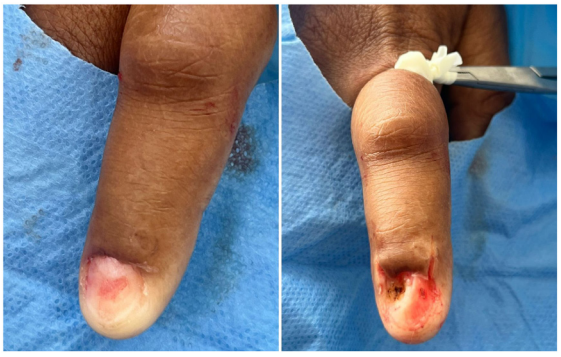

Figure 6. Glomus tumor before and following nail-plate avulsion.

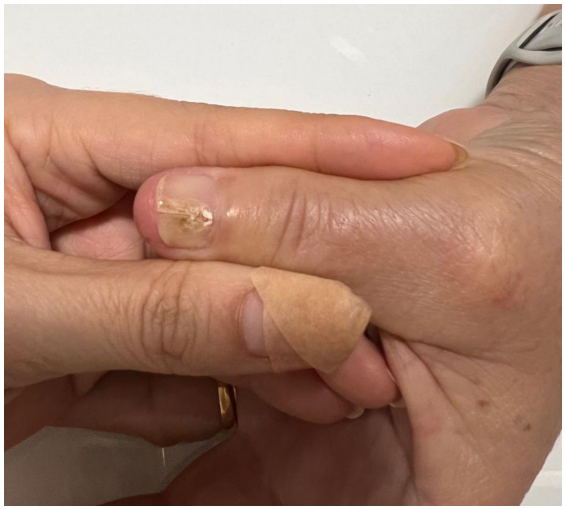

Figure 7. *Onychopapilloma.*

produces an area of blanching larger than expected, an underlying abscess is likely present[31-33].

Paronychia can be classified as acute or chronic[31,33]. In the acute form, physical examination may reveal a tender, erythematous, and edematous lateral nail fold, and if an abscess is present, a fluctuant area may be palpable[31]. In chronic paronychia, the nail fold may be red and swollen, but fluctuation is uncommon; the nail plate may become thickened and discolored, and proximal nail fold retraction, nail dystrophy, and cuticle loss can occur[31].

Benign neoplastic nail disorders

Glomus tumor (GT)

GT is a benign vascular hamartoma originating from glomus cells, specialized smooth muscle cells concentrated around dilated vessels and this tumor present as red, purple, or blue lesions beneath the nail plate, classically characterized by the triad of pain, tenderness, and cold sensitivity[34,35].

Clinical characteristics of GT typically appear as a small reddish-to-bluish macule under the nail plate or as longitudinal erythronychia with distal notching or fissuring of the nail plate[34] (Fig. 6). The predominant symptom is intense nail pain, which may be throbbing or pinpoint in nature; it can occur spontaneously or be provoked by pressure or cold exposure[5,34,35].

GT are generally small and rarely palpable, rendering clinical examination inadequate for precise localization[36]. Imaging studies facilitate accurate tumor localization and size assessment, critical factors in selecting the optimal surgical approach[36,37]. Nail-plate dermatoscopy may reveal vascular structures; however, these can sometimes be subtle or absent[36]. Therefore, dermatoscopy of the nail bed and matrix before tumor excision is recommended, as it assists both in tumor localization and in visualizing the lesion's vascular pattern[36].

Definitive diagnosis is established by performing a nail bed biopsy with nail plate avulsion. Histopathological examination demonstrates a variable admixture of glomus cells, vascular channels, and smooth muscle[38]. GT are subclassified into three types: glomangiomas, marked by an abundance of vascular channels; solid GTs, composed predominantly of glomus cells; and glomangiomyomas, which show a predominance of smooth muscle elements[38].

Onychopapilloma

Onychopapilloma is a benign neoplasm of the distal matrix and nail bed, typically presenting as a longitudinal band of splinter hemorrhages associated with subungual hyperkeratosis[39] (Fig. 7). The most common dermatoscopic finding is longitudinal erythronychia, although melanonychia and a V-shaped distal nail-plate notch may also be observed[39].

Histopathological examination features include subungual hyperkeratosis with or without focal hemorrhage; in excisional specimens, there is papillomatosis of the nail bed and acanthosis of the nail matrix with layers of subungual parakeratosis and focal parakeratosis[39].

Figure 8. Clinical and dermatoscopical images of squamous cell carcinoma.

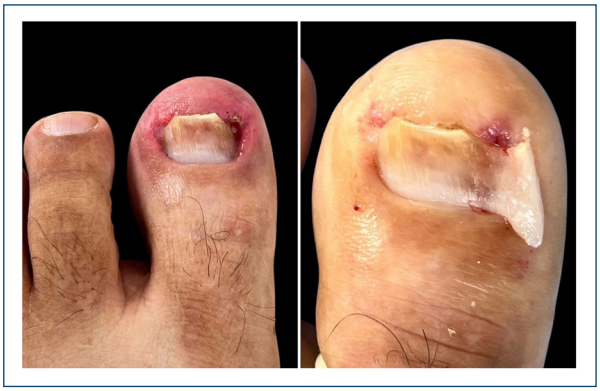

Figure 9. Onychocryptosis.

Malignant neoplastic nail disorders

Subungual melanoma (SM)

SM is a distinct subtype of cutaneous malignant melanoma that arises from the nail matrix. It is usually a variant of acral lentiginous melanoma, a form of melanoma originating in the palmoplantar region[40,41]. In two-thirds of cases, SM presents as a longitudinal brown-to-black band on the nail plate, known as longitudinal melanonychia, but it may also be amelanotic and manifest as a red nodule[40,41]. During its progression, periungual pigmentation may develop, known as Hutchinson's sign, which, while not pathognomonic, is highly suggestive of melanoma, nail dystrophy may also occur, indicating more advanced disease[40]. SM is often mistaken for an infection and initial misdiagnosis of SM occurs in 85% of cases[41]. Dermoscopy assists in distinguishing SM from benign melanocytic pigmented lesions, but biopsy remains the gold standard for diagnosis[41].

Dermatoscopy can reveal a gray-brown to black background with longitudinal lines that are irregular in thickness, spacing, and color, as well as fine pigmented granules, features indicative of a melanocytic origin[40]. The width of the pigmented bands can vary and may progress to total melanonychia[40].

Histologic features suggestive of malignancy include lesion asymmetry, infiltrative margins, a markedly increased number of melanocytes in the basal and suprabasal layers with a high propensity to form compact aggregates, presence of cytologic atypia, and dermal inflammation. Malignant melanocytes have large, atypical nuclei with increased mitotic activity. Identification of melanocytes in the nail plate is diagnostic of melanoma[42]. Invasive SM also exhibits irregularly dispersed dermal nests composed of atypical melanocytes[42].

Squamous cell carcinoma (SCC)

SCC is the most common malignant tumor of the nail unit, with the *in situ* form (Bowen's disease) occurring more frequently than the invasive variant and usually is associated with the Human Papillomavirus (HPV), mainly type 16, 18, 35, and 56[40,43]. It typically involves a single digit, most commonly the thumb[40,43]. The malignancy is usually indolent and painless, affecting the nail bed and periungual regions or both. Lesions are clinically classified into two main categories: periungual type, arising in the epithelium of the nail fold and sulcus and Subungual type, developing in the epithelium of the nail bed[40,43].

Dermatoscopy of SCC is characterized by brown linear dots or a clustered glomerular vascular pattern[40]. Other features include localized subungual hyperkeratosis, erythrochia or leukonychia irregular, lateral detachment (onycholysis), non-parallel longitudinal melanonychia, and splinter hemorrhages[40] (Fig. 8).

Biopsy with histopathological examination is the gold standard for diagnosing SCC[40,43]. The histopathological characteristic findings of this tumor include loss of normal epidermal stratification, dyskeratosis, clusters of large cells with hyperchromatic nuclei, atypical mitosis, and, when associated with HPV, perinuclear vacuolization is typically observed[40,43].

Traumatic nail disorders

Onychocryptosis

Onychocryptosis, also known as ingrown toenails, is a condition in which the lateral nail fold is penetrated by the nail plate's edge, causing pain and difficulty ambulating[44-47]. It is most common in adolescents, young adults, and males[44,46]. The penetration is often

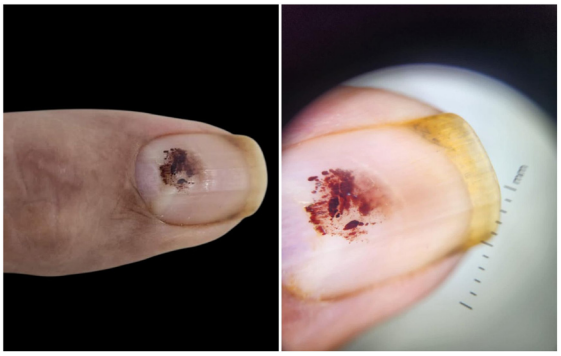

Figure 10. Clinical and dermatoscopy image of subungual hematoma.

due to nail spicules along the plate's margin, which elicit an inflammatory response[44,46,47]. The great toes are most frequently affected[44].

The main causes include ill-fitting footwear, improper toenail trimming, abnormalities of the nail apparatus, and excessive perspiration[44,47]. The condition is unilateral in 80 % of cases and predominantly involves the hallux[44]. Diagnosis of onychocryptosis is straightforward and classically based on clinical features, without the need for laboratory, radiographic studies, or dermatoscopy[44,46,47].

Patients typically present with toe pain that can range from mild discomfort when walking to complete inability to ambulate; depending on lesion progression, there may also be associated swelling, erythema, secondary infection, or seropurulent discharge[44-47] (Fig. 9).

Subungual hematoma (SH)

SH is a common nail lesion characterized by the accumulation of blood beneath a fingernail or toenail, typically located between the nail bed and the nail plate[48]. Trauma is the principal etiology, and the migration of the hematoma distally with nail-plate growth serves as a key diagnostic feature[40,48].

Clinically, the hallmark symptom is sudden, throbbing pain following nail injury, resulting from pressure exerted by the subungual blood collection[48]. SH is the most frequent cause of bluish-red to bluish-black nail pigmentation; unlike melanocytic lesions, it does not form a continuous longitudinal band[40,48,49].

Dermatoscopic examination often reveals small, round blood globules at the periphery of the hematoma, distal streaking, and localized leuconychia at the trauma site, accompanied by a bluish-red, bluish-black, or brownish color coloration[40,48,49] (Fig. 10).

Conclusion

This study analyzed and discussed the two main types of nail conditions in each classification based on their clinical, etiological features and defined objective criteria to recognize each nail lesion. Diagnostic tools, such as dermoscopy, microscopy, culture, and nail biopsy were described, highlighting their importance and clinical applicability for the early diagnosis of some frequent nail diseases. In summary, by systematizing clinical and histopathological criteria for the diagnosis of nail lesions, this study may contribute to reducing diagnostic errors, guide more precise therapeutic management, and improve the quality of life for patients affected by nail disorders.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ORIGINAL ARTICLE

Epidemiological profile of patients with hidradenitis suppurativa at a dermatology service in Southern Brazil

Perfil epidemiológico dos pacientes com hidradenite supurativa em um serviço de dermatologia no Sul do Brazil

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Abstract

Objective: The present study aimed to identify the epidemiological profile, disease severity, and treatments used by patients with HS referred to a specialized dermatology outpatient service at a tertiary hospital in southern Brazil. **Methods**: A cross-sectional observational study analyzing the medical records of patients diagnosed with HS referred to a dermatology outpatient clinic at a tertiary hospital in southern Brazil. Data included both clinical characteristics of the patients and assessment of severity and quality of life scores. **Results**: Ninety-six patients were eligible for the study. Women were predominant, with an average age of 38.4 years. Almost half of the participants were smokers, while 78 % were sedentary and 79 % were overweight. The severity scores showed moderate disease in most patients, significantly impacting quality of life. Patients with symptom onset between the ages of 11 and 20 years had higher DLQI values at diagnosis than the other age groups (p = 0.016). The most commonly used therapeutic by the patients was oral antibiotics associated with topical resorcinol. **Conclusion**: Our findings were similar to those reported by other Latin American and global studies. Early diagnosis, evidence-based treatment, and control of comorbidities are the cornerstones for disease control, offering a better quality of life.

Keywords: Hidradenitis suppurativa. Epidemiology. Brazil.

Resumo

Objetivo: O presente estudo teve como objetivo identificar o perfil epidemiológico, a gravidade da doença e os tratamentos utilizados por pacientes com HS encaminhados a um ambulatório especializado em dermatologia de um hospital terciário do sul do Brazil. **Métodos**: Estudo observacional transversal que analisou os prontuários de pacientes com diagnóstico de HS encaminhados a um ambulatório de dermatologia de um hospital terciário do sul do Brazil. Os dados incluíram as características clínicas dos doentes e a avaliação dos escores de gravidade e qualidade de vida. **Resultados**: 96 doentes foram elegíveis para o estudo. Predominaram as mulheres, com idade média de 38,4 anos. Quase metade dos participantes eram fumantes, enquanto 78% eram sedentários e 79% tinham excesso de peso. Os escores de gravidade mostraram doença moderada na maioria dos pacientes, impactando significativamente a qualidade de vida. Os doentes com início de sintomas entre os 11 e os 20 anos apresentaram valores de DLQI mais elevados no diagnóstico do que os outros grupos etários (p = 0,016).

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A terapêutica mais utilizada pelos pacientes foi a utilização de antibióticos orais associados ao resorcinol tópico. **Conclusão**: Nossos achados foram semelhantes aos relatados por outros estudos latino-americanos e globais. O diagnóstico precoce, o tratamento baseado em evidências e o controle das comorbidades são os pilares para o controle da doença, oferecendo melhor qualidade de vida.

Palavras-chave: Hidradenite supurativa. Epidemiologia. Brazil.

Introduction

Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent, and debilitating cutaneous follicular disease first described in 1839 by Aristide Verneuil[1]. The prevalence in Brazil is 0.41%, similar to the global prevalence of 0.4%[2,3]. North American and European data show a prevalence of 0.7-1.2%, while Garg et al. reported an incidence of 11.4/100,000[4-7]. This high variation is mainly due to the lack of awareness of the disease and ethnic peculiarities among studies[8].

The diagnosis of HS is based on the patient's history and clinical presentation. Symptoms usually emerge after puberty, and the diagnosis is based on three criteria: typical lesions, typical locations, and local recurrence[9]. Characteristic lesions include deep, painful nodules that expand to form abscesses and may progress to suppurative sinus tracts or tunnels, bridging scars, or fistulas. Chronic inflammation leads to fibrosis and contracture, with extensive scarring[10,11]. Commonly affected sites include the axillary, inguinal, gluteal, infra- and intermammary, and perineal regions. The scalp, face, and lower abdomen have been described, but are less frequent sites[12]. The natural history includes periods of inactivity and activation, with two recurrences in 6 months, confirming the diagnosis of HS. Patients usually complain of itching, pain, and local discomfort, exacerbated by physical activity, hair removal, heat, and sweating[11,13].

Risk factors already identified include female gender, smoking, and obesity[14]. Studies on population prevalence and epidemiological profile are scarce, especially in Latin America, although they are essential for formulating public policies on HS. This study aimed to identify the epidemiological profile and severity of clinical manifestations in patients diagnosed with HS who were referred to a specialized dermatology outpatient service at a tertiary hospital in southern Brazil.

Materials and methods

A cross-sectional observational study was conducted based on the analysis of medical records of patients with HS evaluated at a specialized dermatology outpatient service at a tertiary hospital in southern Brazil between March 2020 and November 2022. The study was approved by the local Research Ethics Committee (CAAE: 70248723.5.0000.0020) following Resolution n° 466/2012 of the National Health Council (CNS) and the Helsinki Conventions. The inclusion criteria included individuals aged 18 or over who had complete information in their medical records. Patients considered eligible signed the Informed Consent Form and were included in the study.

The data assessed included gender, age, weight, height, body mass index (BMI), comorbidities, disease severity, impact on quality of life, time until diagnosis, and current treatment for HS. The Hurley classification and the International Hidradenitis Suppurativa Severity Score System (IHS-4) were used to assess the disease severity. The Hurley classification assesses the presence of abscesses, tunnels, and scars, generating a classification in 3 stages of severity (1: absence of fistulas or scars; 2: the presence of fistulas and scars separated from each other; and 3: the presence of interconnected fistulas and scars). The IHS-4 corresponds to a mathematical score in which inflammatory nodules are multiplied by one, while abscesses are multiplied by two and draining fistulas by four. Mild conditions are those scored with up to 3 points, moderate conditions between 4 and 10 points, and severe conditions greater than or equal to 11 points. The dermatology quality of life index (DLQI) was used to assess the impact on daily life, and values greater than ten meant a severe impact on the quality of life.

The data were organized in Microsoft Excel® 2019 spreadsheets and statistically analyzed using IBM SPSS Statistics 29.0.2.0. Categorical data were presented as frequency tables, while quantitative variables were presented as descriptive measures (mean, median, standard deviation, minimum, and maximum). The data were assessed for normality using the Kolmogorov-Smirnov test to verify bivariate statistical relationships. Due to the non-homogeneity of the data, it was analyzed using Pearson's Chi-square test, with a significance level of 5%.

Results

Among the 96 patients assessed, 71 were women, and 25 were men (Table 1) with a mean age of 38.4 years (range 14-68 years with a median of 37 years). The patients' weight ranged from 53.0 to 132.0 kg, with a mean of 81.5 kg and a median of 80.0 kg. The mean height was 164 cm, ranging from 136 to 192 cm, and a median of 165 cm. The patients' BMI averaged 29.8 kg/m², with a range of 20.1-43.0 kg/m² and a median of 29.0 kg/m². The age at onset of symptoms ranged from 1 to 60 years, with a mean of 26.3 years and a median of 24.0 years. The time from symptom onset to diagnosis ranged from 6 months to 50 years, with a mean of 10.6 years until diagnosis.

Regarding lifestyle habits, 44 (46%) patients were active smokers, 75 (78 %) patients did not practice any physical activity, and only 21 (21%) patients reported regular physical activity (Table 1). Forty-five (47 %) patients had no other commodities than HS (Table 1). However, 17 (18%) patients reported treatment for systemic arterial hypertension, followed by 10 (10%) cases of diabetes, and 8 (8%) reported anxiety or depression. Other less commonly identified comorbidities were acne (5%), asthma (4%), dyslipidemia (4%), hypothyroidism (4%), Darier's disease (2%), bipolar disorder (2%), psoriasis (1%), Crohn's disease (1%), HIV (1%), schizophrenia (1%), epilepsy (1%), pulmonary emphysema (1%), rheumatoid arthritis (1%), coronary artery disease (1%), and falciform anemia (1%).

Most patients (61.4%) were classified as Hurley 2 at diagnosis, followed by 27.0% as Hurley 1 and 11.4% as Hurley 3 (Table 1). Forty-one individuals (42.7%) were diagnosed as IHS-4 in the mild stage, followed by 33.3% in the moderate stage and 24% of cases in the severe stage (Table 1). The mean DLQI at the time of HS diagnosis was 12.27 points, with a median of 12.5 points.

Patients with an earlier onset of symptoms, between 11 and 20 years of age, had higher DLQI values at diagnosis than the other age groups ($p = 0.016$). About the Hurley classification, although most patients with symptom onset between 11 and 20 years of age had Hurley 2 at diagnosis, there was no significant difference in the sample with the other age groups and age ranges ($p = 0.858$). There was also no statistically significant difference when comparing the age of symptom onset and the IHS-4 at the HS diagnosis ($p = 0.974$).

Twenty-five percent of the patients evaluated were using topical resorcinol associated with some oral antibiotic at the time of the evaluation, followed by 18 patients (18.7%) using only topical resorcinol, 16 (16.6%) using systemic antibiotics, 16 (16.6%) with Adalimumab, 10 (9.6%) with no treatment. The remaining 12 patients (12.5%) were on topical antibiotics or an association of oral antibiotics with metformin, topical antibiotics with metformin, topical antibiotics with oral antibiotics and metformin, or isotretinoin alone (Table 2).

Table 1. Characteristic of the patients with hidradenitis suppurativa regarding clinical and epidemiological aspects

Variable	n (%)
Gender	
Male	25 (26)
Female	71(74)
Age* (years)	
1-10	8 (8)
11-20	37 (39)
21-30	21 (21)
31-40	12 (13)
41-50	13 (14)
51-60	5 (5)
BMI (kg/m²)	
≤ 25	20 (21)
> 25	76 (79)
Smoking	
Yes	44 (46)
No	52 (54)
Physical activity	
Yes	21 (22)
No	75 (78)
Comorbidities	
Yes	51 (53)
No	45 (47)
Hurley stage	
I	26 (27)
II	59 (61)
II	11 (12)
IHS-4	
Mild	41 (43)
Moderate	32 (33)
Severe	23 (24)

*Age at diagnosis. n: number.

Discussion

HS is a chronic inflammatory disease that generally affects 2-3 times more women than men[7]. Our study showed a predominance of female patients, in a ratio of approximately 2.8:1. Although the real reasons are not yet well established, it is postulated that genetic, hormonal, behavioral factors (such as hair removal), and smoking habits may be implicated in the higher incidence in women[15,16]. The average age identified in

Table 2. Current treatment used by the patients on their first visit

Treatment	n (%)
Topic resorcinol + oral antibiotic	24 (25)
Topic resorcinol	18 (19)
Adalimumab	16 (17)
Oral antibiotics	16 (17)
Topic antibiotics	3 (3)
Topic resorcinol + metformin	2 (2)
Topic resorcinol + metformin + isotretinoin	2 (2)
Isotretinoin	2 (2)
Oral antibiotics + metformin	1 (1)
Oral corticosteroids	1 (1)
Antiseptic soaps	1 (1)
No treatment	10 (10)
Total patients (n)	96

n: number.

this study remained between the second and third decades, confirming the condition's onset in the post-puberty period. This mean age of onset of symptoms, between 18 and 29 years, has already been reported in different population studies[7,17].

The research also showed which comorbidities were most associated with HS in our specialized outpatient dermatology clinic. Obesity, systemic arterial hypertension, insulin resistance, and dyslipidemia were identified. These clinical conditions, which form metabolic syndrome (MS), are related individually or in combination with HS, and the odds ratio for developing MS among patients with HS ranges from 1.82 to 2.37[18-20]. The relationship between the two conditions seems to be linked to chronic inflammatory pathways. Chronic inflammation in HS leads to the development of insulin resistance and, consequently, endothelial dysfunction, promoting cardiovascular disease[19]. Rodríguez-Zuñiga et al., in an Argentinian study, showed that the risk of MS in patients with HS is higher in hospitals than in outpatient settings[19]. It is suggested that patients admitted to wards or emergency rooms have more severe conditions and more inflammation, thus are more likely to develop MS[19]. On the other hand, another study revealed no relationship between the presence of MS and the severity of HS[21]. Therefore, it is difficult to establish if comorbidities lead to the development of a more severe form of MS or if it is the skin condition that, with inflammation, leads to the occurrence of other diseases.

Obesity contributes substantially to systemic inflammation, which may represent a common pathway between HS and MS. Obese patients have twice the risk of developing MS than those who are overweight[22]. On average, the participants in the study had a BMI consistent with overweight, while 79% of the individuals were above the normal BMI. Gold et al. found an 87.6% incidence of obesity among patients with HS[18]. In addition to disrupting the skin barrier, altering sebum production, and promoting systemic inflammation, obesity forms prominent skin folds. Constant friction in flexural areas results in follicular damage, obstruction, and irritation from sweat retention, resulting in a favorable environment for developing HS lesions[23].

Behavior also influences skin disease occurrence, severity, and refractoriness. Data indicates that between 29% and 39% of patients with HS are smokers and that those with HS are twice as likely to be smokers when compared to controls[19,24,25]. The present study showed significantly higher comparative percentages, with 45.8% of the sample comprising smokers while 78.1% were sedentary. Smoking increases inflammation and accelerates the process of atherogenesis, which can feed back into the components of MS, as well as acting as a factor that hinders the response to treatments for HS[26].

In addition to the skin, HS also impacts patients' quality of life due to the high rates of interference in sexual health, self-image, and interpersonal relationships[27]. Scarring, pain, lack of awareness, and delays in treatment lead to psychological suffering, making patients more susceptible to depression, substance abuse, and suicide[24]. The occurrence of depression or anxiety was reported in 8.3% of the patients in the study, which is higher than the average for the Brazilian population[28]. A North American study revealed an eightfold increase in psychiatric illnesses and drug addiction in patients with HS[24]. In the multivariate analysis, it was not possible to verify an increased incidence of alcohol dependence among patients with HS. Shlyankevich et al. then postulated that when adjusting for psychiatric comorbidities, which are more prone to alcohol abuse, the relationship between alcoholism and HS became less clear[24].

Health professionals generally develop severity scores to facilitate clinical assessment. These clinical scores serve as parameters to classify patients qualitatively and quantitatively and work as a tool to measure the severity of the disease and guide therapy.

The correct diagnosis of HS is usually made between 7 and 10 years from the onset of symptoms[14,29]. General practitioners and primary care physicians are frequently at the forefront of diagnosing and managing HS. Many of them still have scarce knowledge about the disease and its impact, and greater awareness of the disease is needed through continuing medical education[30,31]. The dermatologist is the most appropriate specialist for diagnosing HS, playing an important role in reducing the delay in diagnosis. However, because it is a specialized service with limited access, it is not the patient's first physician[14,30]. Raising awareness of the disease among general practitioners and professionals from other medical specialties, through ongoing medical education programs, is an essential strategy in reducing the patient journey until final diagnosis.

When they are finally diagnosed, these patients present with a more severe condition and report a more significant negative impact on interpersonal relationships. In line with this trend, the patients in the study had, on average, scores that reflected a moderate to severe illness with a significant impact on their quality of life. Individuals with an earlier disease onset reported higher DLQIs ($p = 0.016$), reflecting the more significant social impact of HS in adolescents since this age group is more concerned with aesthetics and body beauty and more prone to psychological distress.

Treatment for HS depends on the disease's severity and the patient's characteristics. Disease's chronicity guidance is vital when starting therapy, as patients must be aware that the aim is the control of the lesions and not the cure. The preference for laser hair removal techniques and clothing made of breathable fabrics are adjuvant behavioral measure in the treatment[3,9,16]. Suggesting smoking cessation, regular physical activity, and weight control to reduce the degree of systemic inflammation comprises a series of interventions that seek to act on the main risk factors for HS[9,32].

The first line of drug treatment, especially in mild cases, involves topical antibiotics, which may be associated with keratolytic substances[9,33]. The next step in moderate/severe or refractory cases involves oral antibiotics, especially clindamycin with rifampicin[3,9]. Four patients in the study used isotretinoin alone or in combination with another therapy. This retinoid is no longer among the medications recommended for HS since evidence suggests that it does not benefit the clinical condition and may even worsen it[34,35]. This situation exemplifies how alternative antibiotic therapy regimens or systemic medications are often prescribed due to a lack of technical knowledge or economic issues.

Immunobiological drugs or small molecules can be used to treat unresponsive cases[3]. Among the immunobiological medications is Adalimumab, an inhibitor of tissue necrosis factor-alpha, with robust evidence of safety and efficacy[36]. Following local guidelines, Adalimumab can be prescribed after refractory use of oral antibiotics and topical medications, which justifies its position as the third most prescribed therapy among the patients in the study[37]. Other immunobiological medications and Janus kinase inhibitors are newer drugs that have also shown encouraging results in their ability to control the disease[38-40]. Increasing the therapeutic arsenal results in safer treatment options with fewer adverse effects, but it also increases the cost of treatment for the health system in resemblance to what occurs in psoriasis[41].

Most of the knowledge about HS comes from studies conducted in European countries and the United States. Latin America, however, has a different population profile, with a higher proportion of black and indigenous people. Thus, to more accurately assess the epidemiological profile of HS and its risk factors in Latin American countries, more studies with larger caseloads and the participation of more research centers are needed. Several factors seem to be related to the degree of severity of the disease in HS, such as the time between the onset of symptoms and definitive diagnosis, and the number of professionals needed before the diagnosis of HS is established. Research evaluating these two variables could help measure the health system's quality in adequately diagnosing and treating patients with this condition and measuring the reflection of these delays in higher severity scores.

Conclusion

HS remains a challenging disease, and this study represents an important contribution to the epidemiological assessment of HS patients in a specialized center in southern Brazil. Our findings were similar to those found in Latin American and global literature. Delays in diagnosis and difficulties in establishing effective treatments to control the disease are factors that lead to more severe conditions. In addition, the management of comorbidities such as obesity, smoking, sedentary, and diabetes is crucial so that treatments with topical agents or immunobiological medications, or surgery can be effective and long-lasting.

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None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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Port J Dermatol and Venereol. **ORIGINAL ARTICLE**

Accessing medical knowledge on hidradenitis suppurativa: the impact of continuing medical education on portuguese doctors

Avaliação do conhecimento médico em hidradenite supurativa: impacto da formação médica contínua nos médicos portugueses

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Abstract

Objective: This study aimed to assess Portuguese physicians' baseline knowledge of Hidradenitis suppurativa (HS) and evaluate the role of continuous medical education. **Methods:** A digital continuing education course was created, featuring a lecture and an 8-question assessment. From the 1503 physicians enrolled, a control group of 501 physicians was randomly selected to complete the questionnaire before the course. After the course, the questionnaire was sent to all physicians who attended the lecture and were not part of the control group (381 physicians). **Results:** We collected 131 responses from the control group and 38 from the intervention group. The educational intervention significantly improved physicians' knowledge, as evidenced by higher total scores in intervention group (mean: 90.00) compared to the control group (mean: 79.22; $p < 0.001$). The question regarding the importance of specialist referral showed the greatest improvement, with 89.5% correct responses in the intervention group versus 65.6% in control group ($p = 0.004$). **Conclusion:** This study demonstrates that continuing educational interventions can effectively contribute to improve medical knowledge about HS, particularly concerning appropriate patient referral.

Keywords: Hidradenitis suppurativa. Continuous medical education. Digital medical education.

Resumo

Objetivo: Este estudo teve como objetivo avaliar o conhecimento dos médicos portugueses sobre a HS e avaliar o papel da educação médica contínua na melhoria da compreensão da doença. **Métodos:** Foi desenvolvido um curso de educação médica contínua online, que incluiu uma sessão clínica e um questionário de 8 perguntas. Dos 1503 médicos inscritos, foi selecionado aleatoriamente um grupo controlo de 501 médicos para preencher o questionário previamente ao curso. Após a conclusão da formação, o questionário foi enviado aos médicos que assistiram à sessão clínica e não pertenciam ao grupo controlo (381 médicos). **Resultados:** Foram obtidas 131 respostas no grupo controlo e 38 no grupo de intervenção. A realização da formação melhorou significativamente o conhecimento dos médicos, como evidenciado pelas pontuações totais mais elevadas no grupo de intervenção (média: 90.00) em comparação com o grupo controlo (média: 79.22; $p < 0.001$).

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A pergunta sobre a importância da referenciação para um especialista foi a que apresentou resultados mais expressivos, com 89.5% de respostas corretas no grupo de intervenção e 65.6% no grupo de controlo (p = 0.004). **Conclusão:** Este estudo demonstra que a formação médica contínua pode contribuir efetivamente para melhorar os conhecimentos médicos sobre HS, particularmente no que diz respeito à referenciação adequada dos doentes.

Palavras-chave: Hidradenitis suppurativa. Educação médica contínua. Fomação médica digital.

Introduction

Hidradenitis suppurativa (HS) is a chronic, recurrent, mutilating dermatosis with a significant impact on patients' quality of life[1,2]. It is characterized by follicular destruction in areas rich in apocrine glands, leading to the appearance of inflammatory nodules and abscesses that may progress to fistulas and scarring, particularly in untreated patients[1,3]. Indeed, beyond new discoveries in HS pathogenesis and subsequent therapeutic optimization[4,5], several authors have identified delayed diagnosis as a major challenge in managing HS patients, with many years often elapsing between the onset of initial lesions and clinical diagnosis[6-8].

The delay in the diagnosis of HS is largely due to the difficulty in recognizing the condition by clinicians who are not specialists in this area, and these clinicians are often the first healthcare professionals to observe these patients[6-8]. In Portugal, there has been an ongoing effort to optimize the diagnosis and treatment of HS patients, mainly through continuing medical education sessions and the publication in 2023 of national clinical guidelines to improve patient referrals to dermatology services, facilitating timely diagnosis and treatment[9]. However, it is important to determine whether these guidelines are known and understood by frontline physicians, particularly those in primary care or emergency departments, who are often the first to see HS patients.

In this context, and as part of a continuing education course in dermatology, a survey was conducted among participating physicians both to assess their baseline knowledge of these guidelines and to evaluate the impact of educational interventions on their knowledge. Therefore, the goal of this study was to determine whether targeted training sessions could effectively enhance physician knowledge and bridge the gaps identified in initial assessments. By evaluating the effects of these educational initiatives, we aim to understand their relevance in improving clinical practice, with the ultimate goal of facilitating timely and accurate diagnosis and treatment of HS patients.

Material and methods

To assess the baseline medical knowledge of physicians and the impact of medical e-learning in HS, we used a medical knowledge platform called Dioscope© to create and host our learning course. After course creation and physicians' registration, participants were divided into two groups. Of the 1,503 physicians enrolled in the course, 501 were randomly selected to receive the questionnaire before any educational activity took place (control group). From the remaining participants, all who had attended the training on HS were selected, excluding those who had already been chosen for the initial questionnaire, resulting in a total of 381 physicians to whom the questionnaire was sent (intervention group). This division aimed to minimize bias from physicians who had already answered the questions and, therefore, were familiar with the answers. The goal was to evaluate whether there was a genuine improvement in medical knowledge because of the training.

Physicians were asked to provide a registration record and were grouped according to their medical specialty. Those with incomplete registration records, preventing its correct characterization, were excluded.

The questionnaire included eight questions based on the national HS guidelines (Table 1). Data was analyzed with Statistical Package for the Social Sciences, version 29.0 (IBM Corp., 2023). Categorical variables were presented as frequencies and percentages. Continuous variables were presented as means (M) and standard deviations (SD). Normality was assessed with Kolmogorov–Smirnov ($n > 50$) or Shapiro–Wilks ($n \leq 50$) complemented with quantile-quantile-plots. Score comparison was assessed with independent t-test. Questions comparisons were performed with χ^2 test or Fisher exact test, when Cochran's rules were not met. The effect size for t-test was calculated as Cohen's d, having 0.2 (low), 0.5 (moderate), 0.8 (high) as thresholds and phi (Φ) for χ^2/fisher test, having 0.1 (low), 0.3 (moderate), and 0.5 (high). Thresholds followed Cohen's 1988 recommendations[10].

Table 1. Answer key

Questionnaire	Correct answer
1. HS is characterized by the presence of primary, recurrent, suppurative lesions in the axillae, inguinal folds, perineum, perianal area, buttocks, inframammary folds, and periumbilical region.	True
2. HS usually manifests in childhood, with higher incidence and prevalence in males.	False
3. Chronic inflammation in HS contributes to an increased risk of squamous cell carcinoma in the affected areas.	True
4. The diagnosis of HS should be considered in any paediatric or adult patient with at least two episodes within a 6-month period, or persistent lesions over the same period, involving painful and suppurative lesions in typical areas.	True
5. The diagnosis of HS must always be confirmed by skin biopsy.	False
6. Any individual with suspected HS should be referred to Dermatology or an HS specialist for diagnostic confirmation and treatment guidance.	True
7. Microbiological examination should be routinely requested in patients with suppurative lesions.	False
8. In mild to moderate HS, localized with few and superficial lesions, the use of topical clindamycin 1% twice daily for up to three consecutive months may be considered.	True

HS: hidradenitis suppurativa.

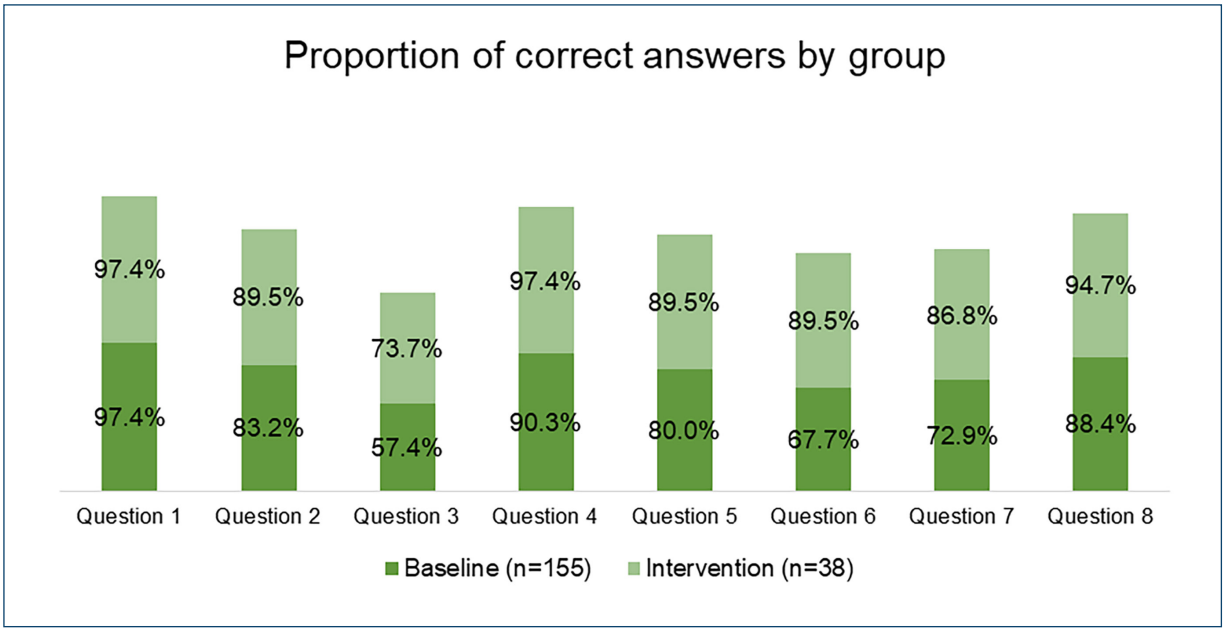

Figure 1. Distribution of the proportion of correct answers by group.

Results

We collected 131 responses from the control group and 38 from the intervention group. Figure 1 and table 2 shows the results for each question, presenting the percentage of correct answers and the corresponding p-values.

The results showed that, for Question 1, 98.5% of participants in the control group answered correctly (129 out of 131), closely followed by the intervention group, with 97.4% (37 out of 38), with no significant difference between groups (p = 0.537). For Question 2, the percentage of correct answers was 83.2% in the control group (109 out of 131) and 89.5% in the intervention group (34 out of 38), with no statistically significant difference (p = 0.449). For Question 3, 58.8% of participants in the control group (77 out of 131) and 73.7% in the intervention group (28 out of 38) answered correctly, with a marginally significant difference observed (p = 0.095). For Question 4, correct responses were provided by 88.5% of the control group (116 out of 131) and 97.4% of the intervention group (37 out of 38), with no significant difference detected (p = 0.125). For

Table 2. Question results of control and intervention groups

Questions	Correct answers of the control group (n = 131) (%)	Correct answers of the intervention group (n = 38) (%)	p	Effect size
Question 1	129 (98.5)	37 (97.4)	0.537†	0.04
Question 2	109 (83.2)	34 (89.5)	0.449*	0.07
Question 3	77 (58.8)	28 (73.7)	0.095*¶	0.13
Question 4	116 (88.5)	37 (97.4)	0.125†	0.13
Question 5	103 (78.6.0)	34 (89.5)	0.133*	0.12
Question 6	86 (65.6)	34 (89.5)	0.004*§	0.22
Question 7	93 (71.0)	33 (86.8)	0.048*‡	0.15
Question 8	115 (87.7)	36 (94.7)	0.369†	0.09

Results presented as n (%).
*χ^2 test.
†Fisher exact test.
‡p < 0.05.
§p < 0.01.
¶p < 0.10.

Question 5, 78.6% of participants in the control group (103 out of 131) and 89.5% in the intervention group (34 out of 38) answered correctly, with no significant difference (p = 0.133). For Question 6, 65.6% of the control group (86 out of 131) and 89.5% of the intervention group (34 out of 38) gave correct answers, with a significant difference favoring the intervention group (p = 0.004). For Question 7, 71.0% of participants in the control group (93 out of 131) and 86.8% in the intervention group (33 out of 38) provided correct responses, with a significant difference noted (p = 0.048). For Question 8, correct responses were observed in 87.7% of the control group (115 out of 131) and 94.7% of the intervention group (36 out of 38), with no significant difference between groups (p = 0.369). Effect sizes were mostly low. Table 3 shows results for score comparison between control and intervention groups.

The total score, obtained by computing the average percentage of correct answers, was higher in the intervention group, with a mean of 90.00 (SD = 10.35), compared to the control group, which had a mean of 79.22 (SD = 14.22). The difference between groups was statistically significant (p < 0.001). The effect size, calculated as Cohen's d, was 0.79, indicating a moderate to high magnitude effect.

The results of the physicians were also analyzed based on the specialty they reported in the login form. In the control group (n = 131), the most represented specialties were Family Medicine (n = 78; 59,5%); Internal Medicine (14; 10,7%); Dermatology (5; 3,8%); Occupational Medicine (4; 3,1%); Pediatrics (4; 3,1%); and General Residency interns (4; 3,1%). Detailed results by specialty are presented in table 4.

Regarding the intervention group, the most represented specialties were Family Medicine (n = 20; 52,6%); Pediatrics (3; 7,9%); Occupational Medicine (3; 7,9%); Internal Medicine (2; 5,2%); and Public Health (2; 5,2%).

Table 3. Score results of control and intervention groups

	Correct answers of the control group (n = 131)	Correct answers of the intervention group (n = 38)	p	Effect size
Total score	79.22 (14.22)	90.00 (10.35)	< 0.001*	d = 0.79

Results presented as M (SD), p value calculated with t-test.
*p < 0.001, effect size calculated as Cohen's d.

Table 4. Control group performance by medical specialty

Specialty	Percentage of correct answers
Dermatology	92.6
Endocrinology	92.0
Pediatrics	87.75
Family medicine	81.46
Internal medicine	77.0
General resident	69.0
Occupational medicine	69.0

Table 5. Question results of control vs. intervention groups in family doctors

Questions	Control (n = 78)		Intervention (n = 20)		p	Effect size
	Incorrect (%)	Correct (%)	Incorrect (%)	Correct (%)		
Question 1	1 (1.3)	77 (98.7)	0 (0.0)	20 (100.0)	> 0.990†	0.05
Question 2	12 (15.4)	66 (84.6)	4 (20.0)	16 (80.0)	0.735†	0.05
Question 3	33 (42.3)	45 (57.7)	6 (30.0)	14 (70.0)	0.316*	0.10
Question 4	8 (10.3)	70 (89.7)	0 (0.0)	20 (100.0)	0.201†	0.15
Question 5	15 (19.2)	63 (80.8)	2 (10.0)	18 (90.0)	0.511†	0.10
Question 6	23 (29.5)	55 (70.5)	4 (20.0)	16 (80.0)	0.397*	0.09
Question 7	17 (21.8)	61 (78.2)	4 (20.0)	16 (80.0)	> 0.990†	0.02
Question 8	8 (10.3)	70 (89.7)	1 (5.0)	19 (95.0)	0.681†	0.07

Results presented as n (%).
*$\chi 2$ test.
†Fisher exact test.

Tables 5 and 6 compare GPs in the control group (n = 78) with those in the intervention group (n = 20), both in individual questions and total scores. In Question 1, both groups scored very highly (98.7% vs. 100.0%; p > 0.990; Φ = 0.05). In Question 2, 84.6% of control group GPs and 80.0% of intervention group GPs answered correctly (p = 0.735; Φ = 0.05). In Question 3, intervention group GPs performed better (70.0% vs. 57.7%), though the difference was not statistically significant (p = 0.316; Φ = 0.10). In Question 4, intervention group GPs answered correctly in all cases (100.0%) compared to 89.7% in the control group (p = 0.201; Φ = 0.15). In Question 5, 90.0% of intervention group GPs answered correctly vs. 80.8% of the control group (p = 0.511; Φ = 0.10), and in Question 6, 80.0% vs. 70.5% (p = 0.397; Φ = 0.09). Question 7 showed nearly identical results (80.0% vs. 78.2%; p > 0.990; Φ = 0.02), and in Question 8, intervention GPs scored 95.0% compared to 89.7% in the control group (p = 0.681; Φ = 0.07). Regarding total score, intervention group GPs had a higher mean of 87.05 (SD = 11.76) compared to 81.25 (SD = 14.35) in the control group. This difference was not statistically significant (p = 0.099), though it approached marginal significance, with a small-to-moderate effect size (Cohen's d = 0.42), indicating a tendency toward better overall performance among GPs in the intervention group, albeit without strong statistical evidence.

Table 6. Score results of control versus intervention groups in family doctors

	Control (n = 78)	Intervention (n = 20)	p	Effect size
Total score	81.25 (14.35)	87.05 (11.76)	0.099*	d = 0.42

Results presented as M (SD), p value calculated with t-test.
*p < 0.10.

Discussion

The results of this study demonstrate a trend toward improved medical knowledge among physicians regarding HS after targeted educational intervention. The educational session, based on national HS guidelines, appeared to effectively enhance participants' understanding, as evidenced by the statistically significant improvement in the overall scores of the intervention group compared to the control group.

The results indicate that the control and intervention groups had comparable compositions, each being predominantly comprised of Family Medicine physicians. When Family Medicine physicians from both cohorts were analyzed separately-after standardizing their baseline characteristics–the intervention-group GPs exhibited a trend toward superior overall performance, although this did not reach statistical significance, thus supporting the study's overall findings.

It is also noteworthy that, by random assignment, the control group included a higher proportion of physicians from specialties with superior baseline performance (e.g., Dermatology), which makes the observed knowledge gains more meaningful.

Upon examining individual question results, Question 6 emerged as a significant indicator of knowledge

improvement. The intervention group showed a higher rate of correct answers (89.5%) compared to the control group (78.6%), with p = 0.004, indicating that participants benefited from the educational session, particularly regarding the importance of referring patients with suspected HS to specialists. These findings are consistent with another study involving Portuguese general practitioners and family medicine physicians[11], which reported a correct referral rate to dermatologists of 75.5%, significantly lower than the correct diagnosis rate of 90%, highlighting a general lack of knowledge regarding appropriate referral for HS[12]. Our data show that targeted medical education can effectively address this gap, improving physicians' referral practices and enabling timely initiation of appropriate therapies, which, in severe cases, may include biotechnological drugs only available in hospital settings.

Additionally, questions addressing the association between chronic inflammation and squamous cell carcinoma (Question 3) and the use of microbiological examination (Question 7) demonstrated marginal improvements, suggesting areas where participants benefited but where gains did not reach statistical significance. The improvement regarding the development of squamous cell carcinoma is particularly relevant due to its significant impact on patient prognosis[13], especially in high-risk individuals, where screening for such tumors in HS-affected areas should be incorporated into their clinical management[14]. Similarly, it is important to acknowledge that HS patients are often overtreated with antibiotics, and differentiation between wound colonization and infection is mandatory to prevent antimicrobial resistance, a major threat in HS patients[15].

Despite improvements in specific knowledge areas, several questions showed no significant differences between the control and intervention groups. This suggests that the theoretical knowledge of HS diagnosis is already well established among Portuguese doctors, as noted by other authors[11], with the main knowledge gap residing in the practical aspects of patient referral and management.

The total score comparison between the control and intervention groups highlights the overall effectiveness of the educational program. The mean score for the intervention group was 90.00 (SD = 10.35), significantly higher than the control group's mean score of 79.22 = 14.22), with a $p < 0.001$. The effect size (Cohen's d = 0.79) suggests that the training had a moderate-to-high impact on overall knowledge improvement. These results underscore the potential value of structured, guideline-based educational interventions in improving the clinical knowledge of healthcare professionals.

Despite these promising findings, the study has several limitations that should be addressed in future research. The relatively small sample size, especially in the intervention group, may restrict the generalizability of the results. In addition, the possibility that participants consulted external resources while completing the questionnaire introduces a potential bias. To enhance future research, larger sample sizes and more objective assessments-such as case-based evaluations or patient management simulations-should be incorporated to provide a more comprehensive evaluation of the educational intervention's impact.

Conclusion

In conclusion, this study demonstrates that targeted educational interventions can effectively enhance physicians' knowledge of HS. Particularly by improving their understanding of proper patient referral.

The marginal knowledge improvement regarding the risk of squamous cell carcinoma in these patients and the rational use of microbiological testing-due to their clinical significance-should particularly be emphasized.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that artificial intelligence was used in the writing of this manuscript.

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ORIGINAL ARTICLE

Exploring the association between acne and metabolic syndrome in patients from North-Eastern India: a cross-sectional study in a tertiary care setting

Explorando a associação entre acne e síndrome metabólica em doentes do nordeste da Índia: um estudo transversal num ambiente de cuidados terciários

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Abstract

Objectives: Acne vulgaris is increasingly considered not just as a dermatological condition, but as a manifestation of broader systemic disturbances, including metabolic imbalance and hormonal dysregulation, with emerging evidence linking it to insulin resistance and metabolic syndrome. This study aimed to evaluate the prevalence of metabolic syndrome and insulin resistance among patients with acne vulgaris in a tertiary care setting in North-Eastern India, and to explore their relation with acne severity, body mass index (BMI), and selected biochemical parameters. **Methods:** A cross-sectional study was conducted in acne patients attending the outpatient department of dermatology at a tertiary care center in North-Eastern India. Clinical grading of acne severity was performed, along with anthropometric assessments and biochemical evaluation, which included serum insulin, fasting glucose, thyroid function, sex hormones, and vitamin D levels. Metabolic syndrome was diagnosed based on standard clinical criteria, and insulin resistance was calculated using the homeostasis model assessment. Associations were analyzed using non-parametric statistical tests, with a significance threshold of $p < 0.01$. **Results:** Among the 73 participants, mean age 22.2 ± 3.85 years, the majority (35.6%, n = 26) with a severe acne, 31.5% (n = 23) were overweight or obese, but only 5.47% (n = 4) met the diagnostic criteria for metabolic syndrome and 6.85% (n = 5) for insulin resistance. Despite the elevated BMI in a subset, no statistically significant association was observed between acne severity and either metabolic syndrome or insulin resistance. **Conclusion:** In this studied population, no significant association was found between acne severity and metabolic syndrome or insulin resistance, and these findings highlight acne's complex and context-dependent pathophysiology. Given the study's limitations (cross-sectional design and lack of matched controls), results should be interpreted within the region's unique clinical and nutritional landscape. Further research is needed in diverse populations, particularly in under-represented regions.

***Keywords*:** Acne vulgaris. Metabolic syndrome. Insulin resistance. Body mass index. Mechanistic target of rapamycin complex 1.

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Resumo

Objectivos: A acne vulgar é cada vez mais considerada não só uma condição dermatológica, mas também uma manifestação de distúrbios sistémicos mais amplos, incluindo o desequilíbrio metabólico e a desregulação hormonal, com evidências emergentes que a associam à resistência à insulina e à síndrome metabólica. Este estudo teve como objetivo avaliar a prevalência da síndrome metabólica e da resistência à insulina entre os doentes com acne vulgar num ambiente de cuidados terciários no nordeste da Índia e explorar a sua relação com a gravidade da acne, o índice de massa corporal e parâmetros bioquímicos selecionados. **Métodos:** Foi realizado um estudo transversal em doentes com acne atendidos no ambulatório de Dermatologia de um centro de cuidados terciários no nordeste da Índia. Foi realizada a classificação clínica da gravidade da acne, juntamente com avaliações antropométricas e bioquímicas, que incluíram a insulina sérica, a glicemia em jejum, a função tiroideia, as hormonas sexuais e os níveis de vitamina D. A síndrome metabólica foi diagnosticada com base em critérios clínicos padrão e a resistência à insulina foi calculada através do modelo de avaliação da homeostasia. As associações foram analisadas através de testes estatísticos não paramétricos, com um limiar de significância de $p < 0.01$. **Resultados:** Entre os 73 participantes, com uma média de idades de 22.2 ± 3.85 anos, a maioria (35.6%, n = 26) apresentava acne grave, 31.5% (n = 23) tinham excesso de peso ou obesidade, mas apenas 5.47% (n = 4) preenchiam os critérios de diagnóstico de síndrome metabólica e 6.85% (n = 5) de resistência à insulina. Apesar do índice de massa corporal elevado num subconjunto, não foi observada uma associação estatisticamente significativa entre a gravidade da acne e a síndrome metabólica ou a resistência à insulina. **Conclusão:** Nesta população estudada, não foi encontrada uma associação significativa entre a gravidade da acne e a síndrome metabólica ou a resistência à insulina, e estes achados realçam a fisiopatologia complexa e dependente do contexto da acne. Dadas as limitações do estudo (desenho transversal e ausência de controlos emparelhados), os resultados devem ser interpretados dentro do cenário clínico e nutricional único da região. São necessárias mais pesquisas em populações diversas, particularmente em regiões sub-representadas.

***Palavras-chave*:** Acne vulgar. Síndrome metabólico. Resistência à insulina. IMC (índice de massa corporal). Alvo mecanístico do complexo 1 da rapamicina.

Introduction

Acne vulgaris is a multifactorial, chronic inflammatory disorder of the pilosebaceous unit. Pathogenesis involves an interplay of factors, including hyperkeratinization of the follicular ostium, increased sebum production, bacterial colonization (primarily by *Cutibacterium acnes*), inflammation, hormonal influences, diet, and genetic predisposition. While many patients with acne present with normal androgen levels, conditions such as polycystic ovarian syndrome (PCOS) and congenital adrenal hyperplasia may lead to androgen excess and acne exacerbation[1].

Metabolic syndrome is a cluster of interrelated conditions, including insulin resistance, central obesity, dyslipidemia, and hypertension, and has been increasingly associated with chronic inflammatory skin disorders, including acne. Both conditions share common pathophysiological mechanisms, such as chronic inflammation, oxidative stress, and hormonal dysregulation[2].

Metabolic syndrome is driven by insulin resistance in muscle, fat, and liver cells, exacerbated by visceral obesity and elevated free fatty acids. This leads to increased glucose, triglycerides, and very low-density lipoproteins, creating a vicious cycle of insulin oversecretion and lipolysis. Oxidative stress from impaired sebum scavenging mechanisms further links lipid abnormalities to metabolic syndrome. Hormonal imbalances secondary to hyperinsulinism and insulin resistance can trigger androgen-dependent skin conditions such as acne and hirsutism. Inflammatory cytokines such as interleukin-17 and Tumor Necrosis Factor alpha (TNF-α) that are implicated in psoriasis and atopic dermatitis[3] may also possibly contribute to a metabolic syndrome in acne. While some studies have reported a higher prevalence of metabolic syndrome among acne patients[4], the overall evidence remains inconsistent. Notably, the role of dietary factors, particularly high glycemic index diets, in acne remains a subject of ongoing debate, with conflicting findings in the literature. In North-Eastern India, where rice and carbohydrate-rich staples predominate, the possibility of this association warrants a closer investigation. There is a lack of data from this geographically and ethnically distinct region of India, where unique dietary patterns and lifestyle factors may influence the development of acne and its potential systemic associations. Understanding and evaluating the relationship between acne and metabolic syndrome in this context may aid in early diagnosis and provide opportunities for

integrated treatment strategies targeting both cutaneous and systemic aspects of the disease.

Methods

A cross-sectional observational study was conducted over a period of 1 year in the dermatology outpatient department of a tertiary care teaching hospital in North-Eastern India, after receiving approval from the Institutional Ethics Committee. All eligible adult patients presenting with acne vulgaris and/or truncal acne were recruited through consecutive sampling after obtaining written informed consent. The exclusion criteria involved patients who were diagnosed with PCOS, female patients with irregular menstruation history, amenorrhea or oligomenorrhea, hirsutism, associated male pattern baldness, pregnancy, and acne patients who have taken isotretinoin in the last 3 months.

A detailed assessment of the patient's demographic profile, clinical history, and clinical evaluation was done based on a predefined *pro forma*. Dietary practices were assessed using a structured 7-day recall method, wherein participants were asked to report the number of servings per week for common food items such as vegetables, fruits, chicken, pork, beef, and fish. Participants also provided information on the primary type of cooking oil used at home (e.g., refined oil, mustard oil). The recall focused solely on weekly serving frequency and oil type; detailed portion sizes or nutrient quantification were not assessed. No validated dietary assessment tool was used, which is acknowledged as a limitation. Physical activity was similarly evaluated using a 7-day recall approach. Patients were asked to report engagement in moderate-intensity activities such as brisk walking, cycling at a regular pace, gardening, vacuuming, and doubles tennis. Data were recorded in terms of frequency (days per week) and approximate duration (minutes or hours per day), based on patient-reported estimates. Body mass index (BMI) was calculated and graded according to the recommendations of the Asia-pacific task force: underweight (< 18.5 kg/m^2), normal weight (18.5-22.9 kg/m^2), overweight (23.0-24.9 kg/m^2), and obesity class I (25.0-29.9 kg/m^2), and obesity class II (≥ 30.0 kg/m^2).

Severity of acne was calculated using the global acne grading system[5] by a single dermatologist, which involves dividing the face (including the forehead, both cheeks, the nose, and the chin), chest, and back into six specific regions. The severity of lesions in each area is rated on a scale from 0 to 4, where 0 indicates no lesions, 1 represents comedones, 2 denotes papules, 3 signifies pustules, and 4 corresponds to nodules. After assigning scores for all six regions, the total score is calculated, which is then used to classify acne severity as mild (1-18), moderate (19-30), severe (31-38), or very severe (> 39). Assessment of laboratory parameters was done after overnight fasting for 8 h and included measurement of blood sugar, lipid profile (cholesterol, triglycerides, and high-density lipoprotein [HDL]), uric acid, thyroid profile (thyroid-stimulating hormone [TSH]), vitamin D3, testosterone, dehydroepiandrosterone sulfate (DHEAS), estradiol, and insulin.

Insulin resistance was defined using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) using the formula: fasting insulin (in micro-units per milliliter) multiplied by fasting glucose (in milligrams per deciliter), then divided by 405. Values exceeding 2.5 were considered to be suggestive of insulin resistance[6].

Metabolic syndrome was diagnosed using the guidelines established by the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III)[7]. The criteria include the presence of any three or more of the following five risk factors:

- Central obesity, indicated by a waist circumference of at least 102 cm for men and 88 cm for women (adjusted for Asian populations to > 90 cm and 80 cm, respectively)
- Triglyceride levels of 150 mg/dL or higher, or the use of medication for elevated triglycerides
- HDL cholesterol levels below 40 mg/dL, or medication for low HDL levels
- A blood pressure of 130/85 mmHg or above, or the use of antihypertensive medication
- A fasting plasma glucose level of 100 mg/dL or higher, or the use of medication to treat diabetes mellitus.

It is important to note that fasting insulin levels are not included in the NCEP-ATP III criteria. Instead, waist circumference is utilized as a surrogate marker, given its strong correlation with insulin resistance[8].

The data were entered in a Microsoft Excel sheet (Microsoft® Excel for Mac Version 16.98 [25060824]) and analyzed using Jamovi software (version 2.6.25.0)[9]. Categorical variables were expressed as absolute frequencies and relative frequencies (percentages), whereas continuous variables were summarized as mean ± standard deviation or median with interquartile range, depending on data distribution. Associations between grades of acne or BMI with categorical variables such as metabolic syndrome and insulin

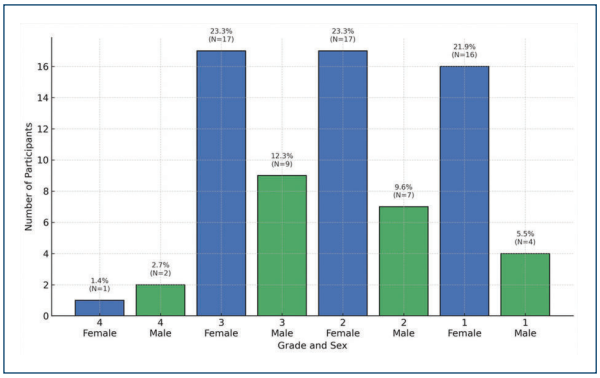

Figure 1. Distribution of acne severity grades by sex.

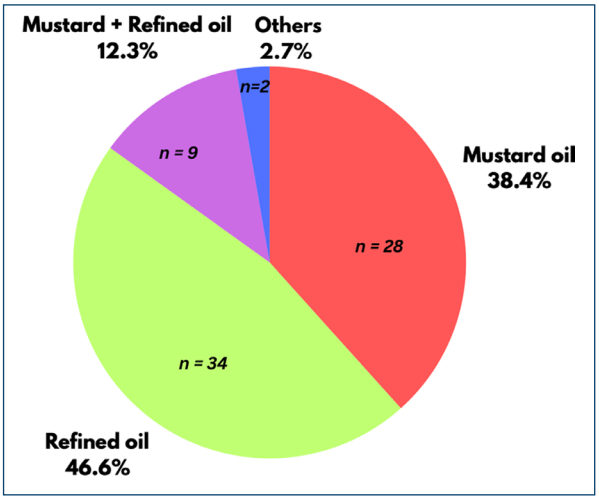

Figure 2. Distribution of cooking oil preferences among study participants.

resistance were assessed using the Mann-Whitney U test. Fisher's exact test was employed to evaluate associations between binary variables due to the small number of positive outcomes. Comparisons of continuous biochemical parameters across acne severity grades were performed using the Kruskal-Wallis test. While logistic and ordinal regression models were considered to explore adjusted associations, they were not performed due to the limited number of outcome events. A $p < 0.01$ was considered statistically significant.

Results

A total of 73 adult patients were included in the study. The patients ranged from 18 to 35 years with a median age of 21 years (interquartile range: 19-25 years) and a mean age of 22.2 ± 3.85. Approximately 70% (n = 51) of the patients were female, with a M:F ratio of 0.43. The majority (82.2%, n = 60) of patients belonged to an urban background.

Acne vulgaris was seen in 50.7% (n = 37), followed by 37% (n = 27) having both acne vulgaris and truncal acne, and the remaining 12.3% (n = 09) had isolated truncal acne. Out of all, the majority (35.6%, n = 26) had a severe grade of acne (Fig. 1). The duration of the disease ranged from 1 month to 15 years, with a median duration of 3 years (interquartile range: 2-5 years).

A positive family history of chronic non-communicable diseases (including diabetes mellitus and hypertension) was found in 39.7% (n = 29). Furthermore, 21.9% (n = 16) and 11% (n = 8) patients gave a history of chronic alcohol consumption and smoking, respectively.Almost 50.7% (n = 37) of patients gave a history of consumption of home-cooked food, out of which 54.8% (n = 40) had three servings and 43.8% (n = 32) had at least two servings. The majority of patients had vegetables on all days of the week with occasional servings of non-vegetarian meals (Table 1). Refined oil and mustard oil were commonly used for home-based cooking (Fig. 2).

Mean moderate physical activity was 1.27 days/week and 11.37 min spent/day (Table 2).

Anthropometry revealed 35.29% (n = 18) of females and 13.63% (n = 3) of males had a waist circumference of ≥ 80 cm and ≥ 90 cm, respectively. Furthermore, 12.32% (n = 9) of patients had a blood pressure of ≥ 130/85 mmHg (Table 2).

The median BMI was 20.93 kg/m^2 (interquartile range: 19.27-23.99 kg/m^2). Among female participants (n = 51), 7 (13.7%) were underweight, 27 (52.9%) had normal weight, 6 (11.8%) were overweight, 9 (17.6%) were classified as Obesity Class I, and 2 (3.9%) as Obesity Class II. Among males (n = 22), 3 (13.6%) were underweight, 13 (59.1%) had normal weight, 2 (9.1%) were overweight, and 4 (18.2%) were classified as Obesity Class I, with none in Obesity Class II. Overall, 8 participants (11.0%) were overweight and 15 (20.5%) were obese, resulting in a combined prevalence of 31.5% with elevated BMI.

The biochemical profile of participants was comprehensively evaluated across acne severity grades. No consistent or clinically meaningful differences were observed in serum uric acid, TSH, DHEAS, insulin, fasting blood glucose, total cholesterol, triglycerides, HDL, estradiol, or testosterone levels (all $p > 0.01$, Kruskal-Wallis test). Only serum vitamin D levels approached statistical significance ($p = 0.011$, Kruskal-Wallis test), though this did not meet the predefined

Table 1. Distribution of weekly servings of major food groups by sex

Servings	Sex	n	Mean	Standard deviation	Minimum	Maximum
Vegetables	Female	51	6.176	1.466	2	7
	Male	22	5.636	1.891	1	7
Fruits	Female	51	3.176	2.260	0	7
	Male	22	2.591	1.894	0	7
Chicken	Female	51	2.157	1.901	0	7
	Male	22	2.136	1.521	0	6
Pork	Female	51	1.176	1.852	0	7
	Male	22	0.227	0.528	0	2
Beef	Female	51	1.078	1.440	0	7
	Male	22	0.909	1.688	0	7
Fish	Female	51	1.588	1.663	0	7
	Male	22	1.682	1.729	0	7

threshold of $p < 0.01$ (Table 3). When categorized using clinical reference standards, vitamin D deficiency (< 20 ng/mL) was observed in 52 participants (71.2%), insufficiency (20-29 ng/mL) in 18 participants (24.7%), and sufficiency (≥ 30 ng/mL) in only 3 participants (4.1%). No cases of vitamin D toxicity were noted.

According to the HOMA-IR criteria, 6.85% (n = 5) of patients had insulin resistance, out of which three were female and had a severe grade of acne. In line with the NCEP-ATP III criteria, 5.47% (n = 4) of patients had metabolic syndrome, out of which half had insulin resistance. However, no statistically significant association was found between acne severity and either metabolic syndrome or insulin resistance (Table 4). A statistically significant association was observed between BMI and the presence of metabolic syndrome ($p = 0.007$, Mann-Whitney U test), with higher BMI values noted among participants with metabolic syndrome. In contrast, the association between BMI and insulin resistance did not reach the predefined threshold for statistical significance ($p = 0.026$), though a trend toward higher BMI in insulin-resistant individuals was noted.

Discussion

Acne vulgaris and metabolic syndrome may share overlapping pathogenic mechanisms, including chronic inflammation, oxidative stress, hormonal dysregulation, and nutrient-sensing pathway disturbances such as elevated mechanistic target of rapamycin complex 1 (mTORC1) activity. Increased mTORC1 signaling, observed in acne-prone skin, has been linked to insulin resistance and obesity, underscoring the complex interplay between dermatological and metabolic pathways[10].

In our study, a total of 73 patients were included. 70% of our patients were female, which was akin to other studies showing a female preponderance[11]. The mean age of our patients was 22.2 ± 3.85, which is similar to another study by Chandak et al., where the mean age was 23.43 ± 3.99 years with predominantly mild to moderate grades of acne; however, in our study, the majority of patients had severe acne (grades 3 and 4)[12]. The predominance of severe acne in this study population may be partly shaped by the nature of a tertiary care setting, where individuals with persistent, distressing, or treatment-refractory acne are more inclined to seek specialized help either through formal referral or personal initiative. In the context of North-Eastern India, this could also reflect broader patterns, where access to early dermatological care is uneven, over-the-counter remedies are commonly used, and visible skin conditions carry a social weight that quietly urges people to seek help only when the burden becomes too much. These are possibilities that merit deeper, community-rooted inquiry.

According to the seven-day recall method, half of our study participants gave a history of consumption of home-cooked meals with a predominant component of vegetables and chicken. Refined oil and mustard oil

Table 2. Distribution of physical activity and anthropometric variables by sex

Variable	Sex	n	Mean	Standard deviation	Minimum	Maximum
Moderate physical activity (minutes/day)	Female	51	3.333	10.280	0	60
	Male	22	30.000	50.710	0	180
Moderate physical activity (days/week)	Female	51	0.765	1.830	0	7
	Male	22	2.455	3.080	0	7
10 min walk (days/week)	Female	51	4.157	3.100	0	7
	Male	22	5.182	2.920	0	7
Walks (minutes/day)	Female	51	36.275	47.460	0	180
	Male	22	55.682	70.670	0	240
Leisure/sitting in a week (hours/day)	Female	51	5.784	2.370	1	12
	Male	22	6.364	2.340	1	12
Waist circumference (in centimetres)	Female	51	80.200	10.690	63	116
	Male	22	78.700	9.320	63	93
Hip circumference (in centimetres)	Female	51	90.700	8.250	73	121
	Male	22	91.400	8.160	73	104
Weight (in kilograms)	Female	51	53.500	10.930	39	99
	Male	22	59.500	9.700	41	79
Height (in centimetres)	Female	51	155.100	5.460	143	168
	Male	22	167.300	5.900	149	178
Systolic blood pressure (mmHg)	Female	51	111.800	9.260	90	138
	Male	22	121.100	16.130	100	180
Diastolic blood pressure (mmHg)	Female	51	73.500	7.490	60	90
	Male	22	80.400	10.320	60	100

were the most commonly used oils for the preparation of food. According to a study by Bansal et al., 23.33% of females gave a history of oily food intake regularly[13]. A high glycemic diet may trigger acne through disrupted nutrient signaling, leading to hyperkeratosis, hyper-seborrhea, and mTORC1 activation, alongside elevated androgen levels[14]. The mean waist circumference in our patients was 79.8 cm, which was comparable to another study by Kaya et al.[15]. Acne in industrialized countries signals aberrant nutrient-driven mTORC1 activation, linked to chronic diseases. Therefore, dermatologists should leverage dietary interventions to mitigate acne and prevent mTORC1-driven conditions[16,17].

The mean moderate physical activity duration in our study participants was approximately 80 min/week, which is inconsistent with the recommended World Health Organization 2020 guidelines on physical activity and sedentary behavior[18]. In the present study, the median BMI of participants was 20.93 kg/m^2 (interquartile range: 19.27-23.99 kg/m^2), with 11.0% classified as overweight and 20.5% as obese, reflecting a combined prevalence of elevated BMI in 31.5% among the participants. Importantly, BMI demonstrated a statistically significant association with metabolic syndrome ($p = 0.007$) and a suggestive trend with insulin resistance ($p = 0.026$), reinforcing the metabolic implications of higher BMI even in a young population. In our study, serum biochemical parameters, including uric acid, TSH, testosterone, estradiol, DHEAS, lipid profile, fasting glucose, and insulin, were largely within normal physiological ranges across both sexes. Notably, no participants demonstrated thyroid dysfunction, suggesting a predominantly euthyroid status in contrast to findings by Bungau et al.[19], where hypothyroidism or

Table 3. Distribution of biochemical parameters by sex with corresponding p-values (Kruskal-Wallis test)

Biochemical parameter	Sex	n	Mean	Standard deviation	Minimum	Maximum	p
Uric acid (mg/dL)	Female	51	4.939	0.913	2.700	7.300	0.727
	Male	22	6.473	1.669	2.900	9.500	
TSH (mU/mL)	Female	51	2.115	1.231	0.790	6.870	0.693
	Male	22	1.668	0.921	0.040	4.530	
Vit. D (ng/mL)	Female	51	17.160	5.382	7.700	34.210	0.011
	Male	22	18.153	6.637	10.600	34.210	
Estradiol (pg/mL)	Female	51	129.843	96.615	28.000	506.000	0.778
	Male	22	53.364	23.114	20.000	123.000	
Testosterone (ng/dL)	Female	51	0.974	1.467	0.130	6.790	0.154
	Male	22	4.183	2.747	0.190	7.870	
DHEAS (mcg/dL)	Female	51	202.625	86.982	54.900	404.900	0.744
	Male	22	271.777	171.668	77.300	832.400	
Total cholesterol (mg/dL)	Female	51	141.588	32.344	76.000	231.000	0.152
	Male	22	133.455	25.069	73.000	176.000	
Triglycerides (mg/dL)	Female	51	77.980	27.335	37.000	170.000	0.989
	Male	22	102.818	40.086	43.000	169.000	
HDL (mg/dL)	Female	51	49.392	8.300	32.000	69.000	0.099
	Male	22	42.773	9.938	27.000	62.000	
FBS (mg/dL)	Female	51	82.588	7.052	70.000	110.000	0.769
	Male	22	83.000	8.608	61.000	101.000	
Insulin (mIU/L)	Female	51	5.749	2.891	1.710	14.920	0.628
	Male	22	5.642	0.913	1.260	7.300	
HOMA-IR score	Female	51	1.184	1.669	0.312	9.500	-
	Male	22	1.208	1.231	0.236	6.870	

TSH: thyroid-stimulating hormone; DHEAS: dehydroepiandrosterone sulphate; HDL: high-density lipoprotein; FBS: fasting blood sugar; HOMA-IR: homeostasis model assessment of insulin resistance.

autoimmune thyroiditis was frequently observed among acne patients. However, vitamin D levels were generally low in our study population, with only three participants falling within the normal range. This aligns with a recent meta-analysis by Hasamoh et al.[20], which found significantly lower serum vitamin D levels in acne patients compared to healthy controls and a negative correlation between vitamin D levels and acne severity. While these findings suggest a potential role of vitamin D in acne pathogenesis, our results highlight the importance of interpreting laboratory data within a broader clinical and contextual framework, especially in populations where baseline hypovitaminosis D may be widespread due to lifestyle or geographic factors, rather than assuming direct causality.

As per the HOMA-IR criteria and NCEP-ATP III, 7% patients had insulin resistance and 5.47% had metabolic syndrome, respectively; however, there was no significant association with acne severity. It was albeit not in consonance with other studies, which showed a statistically significant association between acne, metabolic syndrome, and/or insulin resistance[21-24]. However, this may be attributed to the overall low prevalence of metabolic syndrome in the north eastern part of India, which is supported by a study by Meher and Sahoo, revealing the states of Meghalaya and Assam

Table 4. Statistical associations between clinical variables and metabolic outcomes

Association tested	Statistical test	p
Grade versus metabolic syndrome	Mann-Whitney U	0.069
Grade versus insulin resistance	Mann-Whitney U	0.305
BMI versus metabolic syndrome	Mann-Whitney U	0.007
BMI versus insulin resistance	Mann-Whitney U	0.026
Sex versus metabolic syndrome	Fisher's Exact	0.579
Sex versus insulin resistance	Fisher's Exact	0.634

BMI: body mass index.

to have the lowest prevalence of metabolic syndrome in the case of females (0.5%) and males (0.4%) respectively. In the same study, overall north-eastern India showed a prevalence of metabolic syndrome to be 0.7% in females and 0.5% in males[25].

Several limitations must be acknowledged when interpreting our findings. First, the heterogeneous distribution of acne severity among participants may have diluted potential associations, especially in the absence of a control group. Second, the dietary data were collected using a 7-day recall period without a validated assessment tool, introducing potential recall bias and limiting the precision of dietary intake estimates. Third, the lack of age- and sex-matched healthy controls restricts our ability to draw definitive comparisons. These factors, combined with the cross-sectional design and relatively small sample size, suggest that our findings should be interpreted with caution and not extrapolated beyond the studied population. Future longitudinal studies with standardized dietary assessments and appropriate control groups are warranted to provide deeper insights into the metabolic underpinnings of acne, especially within diverse regional populations such as those in North-East India.

Conclusion

In this study from a tertiary care centre in North-Eastern India, no significant association was found between acne severity and metabolic syndrome or insulin resistance. Although over 30% of participants were overweight or obese, and vitamin D deficiency was widespread, these factors did not show a consistent association with acne severity. These findings highlight the multifactorial nature of acne, shaped by intricate metabolic and nutritional influences that may vary across populations. Given the study's cross-sectional design, modest sample size, and absence of validated dietary tools or matched controls, the results should be interpreted within the unique clinical and nutritional landscape of North-Eastern India, without extrapolation to broader populations. Further longitudinal research is warranted to unravel these associations in more depth, especially in under-represented regions.

What does the study add?

This study contributes to evaluating the relationship between acne vulgaris and metabolic syndrome in patients from North-Eastern India, a population largely under-represented in dermatologic-metabolic research. Even though many participants presented with severe acne, the study did not identify a meaningful link with metabolic syndrome or insulin resistance. These findings challenge assumptions of universal dermato-metabolic linkage and emphasize the influence of regional variables, including diet, physical activity, and metabolic profile, on systemic inflammatory pathways in acne, along with underscoring the importance of conducting broader, multi-regional studies across ethnically and culturally diverse populations to better understand the potential metabolic underpinnings of acne.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied

with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

Confluent and reticulate papillomatosis of Gougerot-Carteaud treated with azithromycin with excellent results

Papilomatose confluente e reticulada de Gougerot-Carteaud tratada com azitromicina com excelente resultado

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Abstract

Confluent and reticulated papillomatosis (CRP) of Gougerot and Carteaud is a rare dermatological condition characterized by diffuse papillomatosis with a reticulated and confluent pattern. It is more commonly observed in individuals with darker skin and can cause significant aesthetic and psychological discomfort due to its persistent and expansive lesion patterns. This condition is often resistant to conventional treatments, making the search for alternative therapies an area of interest. We present a case of CRP treated with azithromycin, highlighting the efficacy and safety of this antibiotic in managing the condition.

Keywords: Gougerot. Carteaud. Papillomatosis. Reticulate. Treatment. Diagnosis.

Resumo

A Papilomatose Confluente e Reticulada de Gougerot e Carteaud é uma condição dermatológica rara caracterizada por uma papilomatose difusa com padrão reticulado e confluente. É mais comumente observada em indivíduos de pele escura e pode causar desconforto estético e psicológico significativo devido ao seu padrão de lesões persistentes e expansivas. Esta condição é frequentemente resistente ao tratamento convencional, tornando a busca por terapias alternativas uma área de interesse. Apresentamos um caso de Papilomatose Confluente e Reticulada tratada com azitromicina, destacando a eficácia e segurança deste antibiótico na gestão da condição.

Palavras-chave: Gougerot. Carteaud. Papilomatose. Reticulada. Tratamento. Diagnostico.

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Introduction

Confluent and reticulated papillomatosis (CRP) of Gougerot and Carteaud is a rare dermatosis characterized by hyperpigmented papules with a slightly verrucous surface, which tends to coalesce into a reticulated pattern. This condition predominantly affects young individuals, with a higher prevalence in women and people with darker skin tones[1]. The lesions are commonly located on the upper trunk, particularly in the interscapular, sternal, and inframammary areas, but may extend to the neck and other regions.

Although the exact etiology of CRP is not yet fully understood, genetic, environmental, and hormonal factors are believed to play significant roles. The disease is chronic and usually asymptomatic, although some patients may report mild pruritus in the affected areas[2]. Histologically, CRP is characterized by acanthosis, papillomatosis, and mild hyperkeratosis without significant inflammatory changes.

The diagnosis is generally clinical, based on the characteristic appearance of the lesions. Dermoscopy and skin biopsy can be helpful in atypical cases to confirm the diagnosis and rule out other pigmented dermatoses, such as acanthosis nigricans and pigmented lichen planus[3]. Treatment options for CRP include topical agents, such as retinoids and keratolytics, as well as systemic therapies for more extensive cases, although treatment response can be variable, and recurrence is common.

Azithromycin, a macrolide widely used in bacterial infections, has shown potential for improving CRP symptoms due to its ability to modulate the inflammatory response. Studies and case reports have demonstrated that azithromycin can provide significant relief of papillomatous lesions and improve the quality of life of patients affected by this condition[4].

In this context, this study reviews the use of azithromycin in the treatment of CRP of Gougerot and Carteaud, highlighting its efficacy and outcomes in patients who did not respond adequately to conventional therapies. The approach aims to provide a comprehensive perspective on the effectiveness of azithromycin as a therapeutic alternative for managing this challenging dermatological condition.

Case report

A 19-year-old obese male patient presented with a 3-year history of brownish plaques, initially appearing on the anterior trunk and progressively spreading to the back, neck, and cubital fossae. The patient denied pruritus, pain, or other associated symptoms, as well as any prior treatments. On dermatological physical examination, plaques composed of punctate, brownish papules, confluent at the center with a reticulated peripheral pattern, were observed on the anterior and posterior neck, intermammary region, epigastrium, back, and bilateral cubital fossae (Figs. 1A and B).

The primary diagnostic hypothesis was CRP of Gougerot-Carteaud. Treatment was initiated with azithromycin 500 mg orally once daily for three consecutive days per week, with a pause for the remaining days, over a total duration of 6 weeks. The condition showed complete resolution within 3 months (Fig. 2A). The patient was followed for a period of approximately 12 months, without recurrences.

Discussion

Conventionally, the management of CRP involves the use of topical treatments, such as retinoids and keratolytics, but the response to these therapies can be inconsistent, with frequent recurrences[3]. In recent years, azithromycin, a macrolide antibiotic, has emerged as an effective option for the treatment of CRP, likely due to its anti-inflammatory and immunomodulatory properties, in addition to its antimicrobial activity. The use of azithromycin in intermittent doses has shown promising results, with reports of significant clinical improvement in patients refractory to other forms of treatment[4].

Studies suggest that azithromycin may reduce inflammation and inhibit bacterial proliferation, which hypothetically could contribute to the pathogenesis of CRP. Furthermore, azithromycin's prolonged action, due to its long half-life, allows for convenient dosing regimens, such as weekly administration, improving treatment adherence[4].

A study conducted by Engin et al. reported that patients treated with azithromycin experienced significant improvement in skin lesions after a short treatment period, with few side effects. This makes azithromycin an attractive alternative, especially in cases where topical treatments are ineffective or poorly tolerated. However, it is important to note that treatment responses may vary, and recurrence, though less common, can still occur, suggesting the need for long-term follow-up[4].

Other case studies report successful treatment of CRP of Gougerot-Carteaud with azithromycin. In Brazil (2008), a 28-year-old male patient was treated with 500 mg of azithromycin for three consecutive days in weekly cycles for six weeks, showing satisfactory

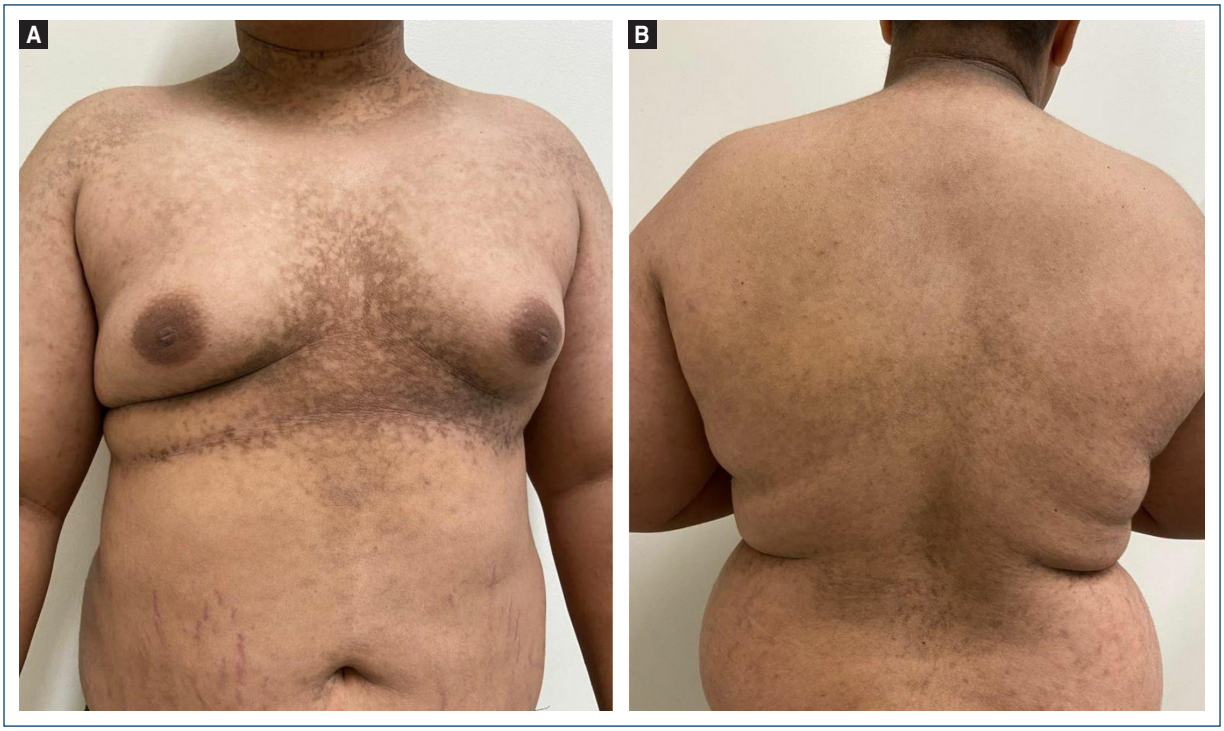

Figure 1. A: brownish papules, more grouped in the center and scattered on the periphery, located on the anterior trunk of an untreated patient. **B:** brownish papules, more grouped in the center and scattered on the periphery, located on the posterior trunk of an untreated patient.

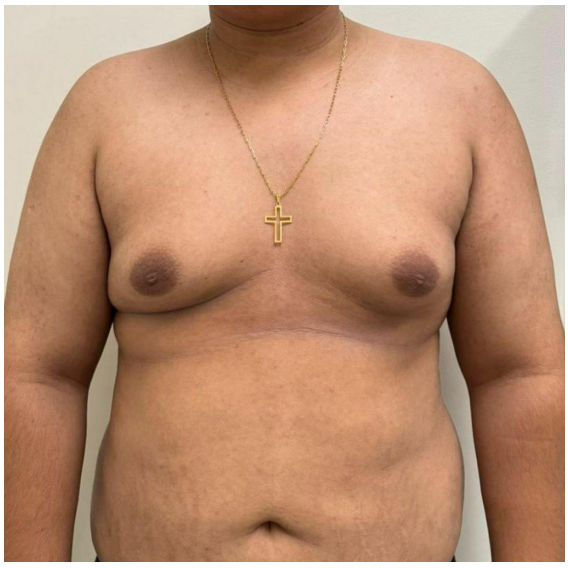

Figure 2. Anterior trunk without papulomatosis lesions, after treatment with azithromycin.

improvement[5]. In 2021, another Brazilian case involving a 19-year-old male patient treated with CRP with the same regimen combined with topical urea and ammonium lactate, resulting in complete remission after 8 weeks[6]. In Turkey (2013), a 16-year-old female patient used 250 mg of azithromycin daily for 12 days, with significant improvement in lesions and no recurrence after 3 months[7].

Conclusion

Despite promising results, the use of azithromycin for CRP still requires further controlled studies to establish its long-term efficacy and determine the optimal dosage regimen. Moreover, since the exact mechanism by which azithromycin benefits CRP patients is not fully understood, additional research is necessary to better understand the disease's pathophysiology and optimize therapeutic approaches[8,9].

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

Significant improvement of refractory cutaneous lesions of lupus erythematosus with the use of anifrolumab: a report of two cases

Melhoria significativa de lesões cutâneas refratárias de lúpus eritematoso com o uso de anifrolumab: relato de dois casos

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Abstract

Anifrolumab, a monoclonal antibody targeting the interferon-1 receptor, is currently approved for the treatment of moderate-to-severe systemic lupus erythematosus, but emerging evidence highlights its potential efficacy in cases with predominant cutaneous involvement. We present two cases illustrating its beneficial impact in refractory cutaneous lupus erythematosus, including both the subacute and chronic subtypes.

Keywords: Cutaneous lupus erythematosus. Discoid lupus erythematosus. Anifrolumab. Subacute cutaneous lupus erythematosus.

Resumo

O anifrolumab, anticorpo monoclonal contra o recetor do IFN-1, encontra-se aprovado para o tratamento do lúpus eritematoso sistémico moderado a grave, mas tem demonstrado evidência crescente de eficácia em doentes com predomínio de envolvimento cutâneo. Apresentamos dois casos ilustrativos do seu impacto benéfico em doentes com lúpus eritematoso cutâneo refratário, incluindo os subtipos subagudo e crónico.

Palavras-chave: Lúpus eritematoso cutâneo. Lúpus eritematoso discóide. Anifrolumab. Lúpus eritematoso cutâneo subagudo.

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Introduction

The therapeutic landscape of cutaneous lupus erythematosus (CLE) remains limited, with hydroxychloroquine and glucocorticoids constituting the only drugs approved by the US food and drug administration (FDA) for this condition[1]. Anifrolumab, a monoclonal antibody targeting the type I interferon (IFN)-1 receptor, was approved in 2022 by the European Medicines agency (EMA) for the treatment of moderate-to-severe systemic lupus erythematosus (SLE) in adults who do not respond to standard therapy. Nevertheless, growing evidence indicates its potential role and efficacy in patients with skin involvement[2-4]. We present two cases highlighting the efficacy of anifrolumab in lupus patients with predominant cutaneous disease.

Case reports

Case 1

A 51-year-old woman with a 4-year history of lupus erythematosus with hematologic and cutaneous involvement was evaluated in our dermatology outpatient department due to discoid lupus lesions affecting the face, trunk, arms, and hands, along with occasional oral ulcers (Figs. 1A-C). Laboratory tests revealed positivity for antinuclear antibodies (titer > 1:640, speckled pattern), lymphopenia and thrombocytopenia (with lowest values of 870×10^9/L and 96×10^9/L, respectively). The cutaneous lesions were refractory to topical and oral corticosteroids, topical calcineurin inhibitors, hydroxychloroquine, azathioprine, and methotrexate. The patient had a SLE disease activity index 2000 (SLEDAI-2K) score of 6 (lymphopenia, thrombocytopenia, new-onset cutaneous lesions, and oral ulcerations), a cutaneous LE disease area and severity index (CLASI) activity score of 26 (involvement of the face, neck, trunk, arms, and hands, with 19 points for areas of bright-red erythema, 6 points for scaly/hypertrophic lesions, and 1 for mucosal involvement), and CLASI damage score of 8 (due to scarring/dyspigmentation of the face, v-area of the neck, and cervical area/back). Treatment with anifrolumab was initiated (intravenous administration of 300 mg every 4 weeks), leading to marked improvement of the cutaneous lesions after the first dose. In fact, at week 12, only scarring from previous lesions remained, with a CLASI activity score of 0 (Figs. 1D-F). The patient currently completed 9 months of treatment, with a sustained cutaneous and hematological response. The patient reported no treatment-related adverse reactions.

Case 2

A 50-year-old woman diagnosed with SLE at the age of 20, with articular and cutaneous involvement, was followed in our dermatology outpatient department for subacute lupus on the trunk and vasculopathy of the extremities, with severe Raynaud's phenomenon, episodic digital ulcers, and nail dystrophy (Figs. 2A and B). Laboratory tests revealed positivity for antinuclear antibodies (titers of 1:1000 with a homogeneous pattern, and 1:320 with a nucleolar pattern), as well as anti-SSa and anti-dsDNA antibodies. Over the preceding 4 years, she experienced worsening of her cutaneous symptoms, remaining corticosteroid-dependent (10-20 mg of prednisolone daily) and showing no response to antimalarials (chloroquine and hydroxychloroquine), calcium channel blockers, pentoxifylline, mycophenolate mofetil, or azathioprine. The patient maintained a SLEDAI-2K score of 12 (positive anti-dsDNA antibodies, new-onset cutaneous lesions, and periungual infarctions), CLASI activity score of 9 (bright red or violaceous erythema of the v-area of the neck, chest, cervical area, and hands), and CLASI damage score of 1 (due to scarring of the hands). She started treatment with anifrolumab (300 mg/monthly), resulting in complete resolution of trunk lesions and improvement in hand vasculopathy and nail dystrophy after 4 months (Figs. 2C and D). The patient recently completed 18 months of therapy, maintaining gradual improvement in ungual and digital involvement and no treatment-related adverse reactions.

Discussion

CLE is a heterogeneous entity encompassing a wide spectrum of clinical manifestations, with its three main subtypes–acute, subacute, and chronic CLE–implying diagnostic, prognostic, and therapeutic particularities[5]. The therapeutic armamentarium, however, is still insufficient regarding the different forms of the disease, without a significant progress over the past decades. Nevertheless, in recent years, new therapeutic targets emerged, such as interferon-receptor antagonism, JAK/STAT inhibition, plasmacytoid dendritic cell-targeted therapies, cereblon-targeting ligands, and B- and T-cell-targeted therapies[1]. In the latter, belimumab, a monoclonal antibody inhibiting B-cell activation, was approved for the treatment of SLE. A meta-analysis of studies of patients with CLE (with or without SLE) demonstrated pooled odds of clinical response at 52 weeks 44% higher in belimumab users compared to non-users[6], hinting its

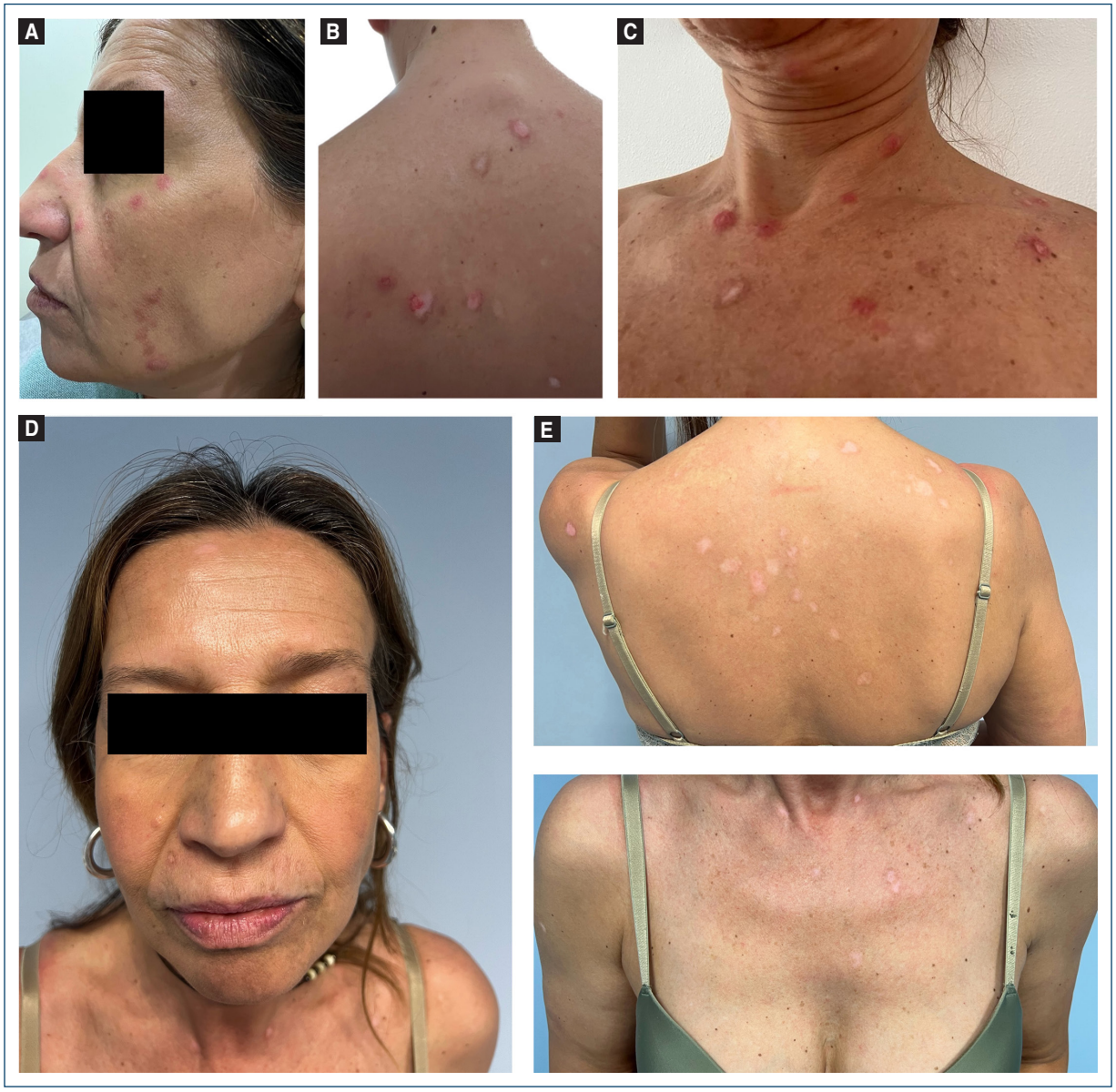

Figure 1. A-C: patient's lesions before, **D-F:** and 6 months after anifrolumab initiation.

potential efficacy in these patients. Furthermore, a phase III trial assessing its efficacy in refractory cutaneous manifestations is currently underway[1]. Litifilimab, a monoclonal antibody binding to BDCA2 (a receptor specific to the surface of plasmacytoid dendritic cells), exhibited significant improvements of CLASI activity score in a phase II trial[7], with other phase II and III trials currently ongoing[1]. Deucravacitinib, a tyrosine kinase-2 inhibitor, showed promising results in CLASI activity score reduction in a phase II trial of SLE patients[8], with an ongoing phase II trial focusing on CLE patients[1]. Anifrolumab, on its turn, received approval for the treatment of SLE by the FDA in 2021 and by the EMA in 2022, based on results from the MUSE, TULIP-1, and TULIP-2 trials[1]. In the MUSE trial, the percentage of patients with a baseline CLASI activity score of ≥ 10 who had a ≥ 50% reduction at week 52 was greater for anifrolumab (63.0% for 300 mg, p = 0.013, and 58.3% for 1,000 mg, p = 0.077) in comparison with placebo (30.8%)[9]. In the TULIP-1 trial, this reduction of ≥ 50%, but assessed at week 12, was achieved by 42% and 25% of anifrolumab (300 mg) patients and placebo group, respectively, without reaching statistical significance. In addition, in the TULIP-2 trial, the same reduction occurred at week 12 in 49% and 25% of patients receiving anifrolumab and placebo, respectively

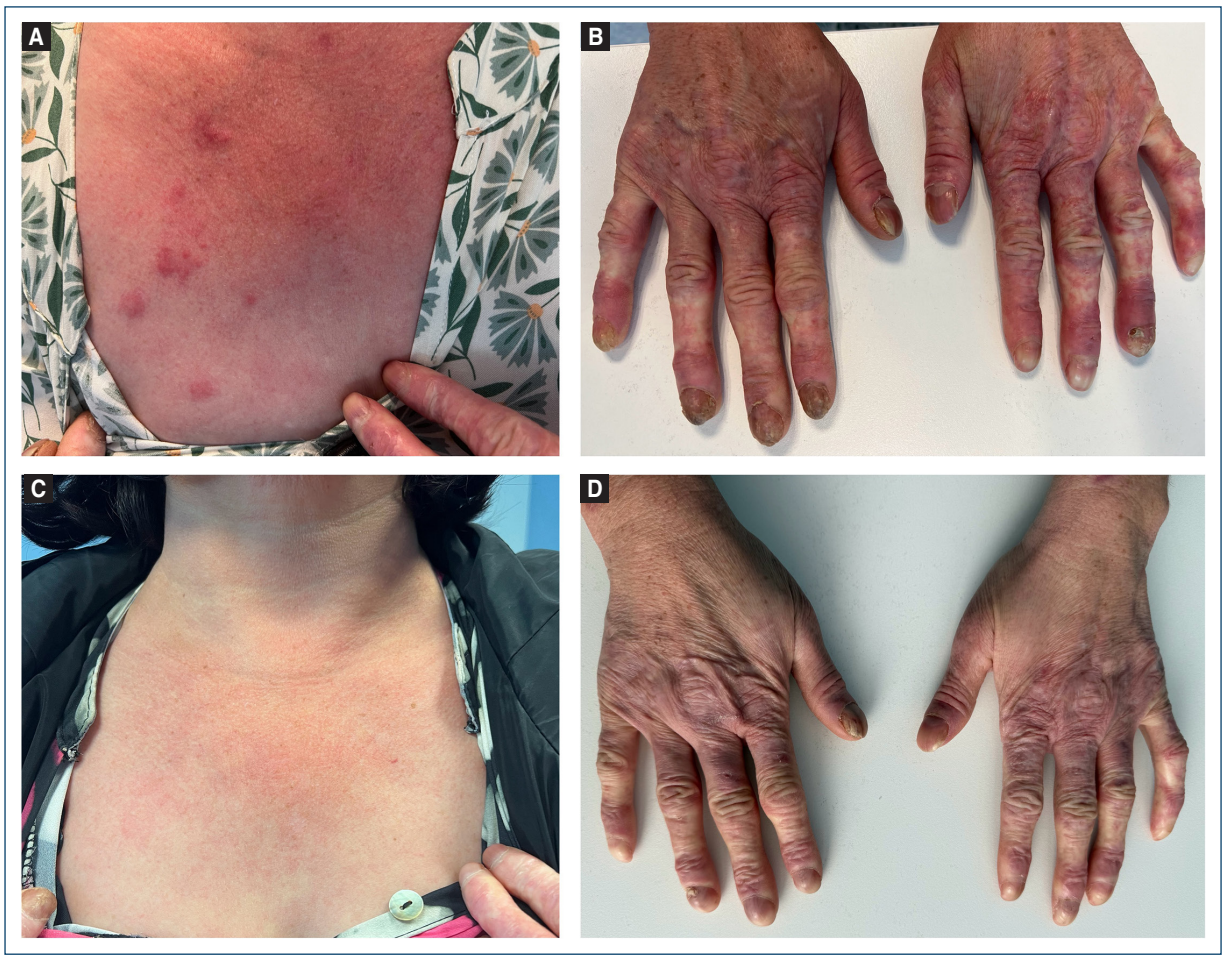

Figure 2. A and **B:** patient's lesions before, **C** and **D:** and 12 months after anifrolumab treatment.

(p = 0.04). A phase III trial is currently being conducted to evaluate the efficacy of anifrolumab in refractory CLE patients (LAVENDER trial)[1]. In parallel with clinical trials, many case reports and case series were published reporting the efficacy of anifrolumab in different variants of CLE, ranging from the acute to subacute (including Rowell syndrome), and chronic subtypes (including discoid lupus, lupus *tumidus*, lupus panniculitis, and chilblain lupus), as well as in associated features such as alopecia and mucosal involvement[3,4,10-12]. Our cases reinforce the beneficial effects of this drug in patients with predominant cutaneous involvement, both in subacute and chronic lupus lesions, with prompt improvement and positive impact on the patient's quality of life, in a field with significant unmet therapeutic needs.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the Institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

The diagnostic perplexity of zosteriform cutaneous metastasis in breast carcinoma

A perplexidade diagnóstica da metástase cutânea zosteriforme no carcinoma de mama

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Abstract

The word "zosteriform" refers to the dermatomal distribution of lesions which can be present in continuous or interrupted bands of one, two, or more contiguous dermatomes unilaterally. Though the dermatomal involvement is highly characteristic of herpes zoster, all lesions presenting in a dermatomal fashion are not herpetic. Differentials such as zosteriform cutaneous metastasis should be considered especially if a patient has an underlying malignancy. Here we report two such rare cases of zosteriform cutaneous metastasis due to underlying breast carcinoma where the patients were being treated on grounds of herpes zoster due to similarities between both these diseases, but the final diagnosis was inconsistent with that.

Keywords: Zosteriform cutaneous metastasis. Herpes zoster. Breast carcinoma.

Resumo

A palavra "zosteriforme" refere-se à distribuição dermatomal das lesões que podem estar presentes em áreas contínuas ou interrompidas de um, dois ou mais dermátomos contíguos unilateralmente. Embora o envolvimento dermatomal seja característico do herpes zoster, nem todas as lesões que se apresentam de forma dermatomal são herpéticas. Diagnósticos diferenciais como metástase cutânea zosteriforme devem ser considerados, especialmente, se o paciente tiver uma doença maligna subjacente. Relatamos dois casos raros de metástase cutânea zosteriforme devido a carcinoma de mama subjacente, em que os pacientes foram tratados como herpes zoster devido a semelhanças entre ambas as doenças.

Palavras-chave: O diagnóstico final. No entanto. Foi de metastização cutânea.

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Introduction

Cutaneous metastasis is a common manifestation of the underlying visceral malignancy[1]. The incidence of skin metastasis varies from 2% to 9% in a primary malignant tumor[2,3]. Breast cancer is the most common cancer associated with cutaneous metastasis after melanoma[4]. This metastasis can result from lymphatic embolization, hematogenous, or from direct implantation[5]. It usually presents in the form of solitary to multiple nodules. Rarely, it can present in a zosteriform pattern with only a few cases, which have been described in the literature[6]. Out of this, only about twelve cases of zosteriform cutaneous metastasis due to underlying breast carcinoma have been described so far[7].

Case report

Case 1

A 49-year-old female patient was referred from the oncology department to the dermatology outpatient department (OPD). The patient reported the appearance of multiple grouped vesicles and nodules on the right side of the breast associated with excruciating pain. She was a known case of Grade three infiltrating ductal adenocarcinoma of the right breast for 2 months, having T4N3M0 stage, for which she had undergone three cycles of Neo adjuvant chemotherapy with Epirubicin, Cyclophosphamide, and 5-Fluorouracil, and was due for the fourth cycle.

On dermatological examination, the patient had multiple grouped vesicles and nodules coalescing to form plaques in a dermatomal distribution, superimposed with erosions and crusting at some sites on the right side of the breast, associated with hyperpigmentation of surrounding skin along with peau d' orange appearance around nipple and areola (Fig. 1A and B). The lesions measured 2-3 cm and were tender on palpation. The patient was treated for Herpes zoster with tablet Acyclovir 800 mg 5 times a day along with anti-inflammatory analgesic medications and tablet Amitriptyline/Pregabalin combination for neuropathic pain, but the lesions were persistent even after 14 days of treatment. On follow-up, similar lesions were found to be spreading over the right arm, right shoulder, and right inframammary region.

Dermoscopy revealed yellow areas, polymorphic vessels, whitish bright lines, and white structureless areas (Fig. 1C).

All routine investigations were within normal limits.

HPE of skin biopsy showed a dermis infiltrated by hyperchromatic pleomorphic nuclei with cells having increased nuclear:cytoplasmic ratio (Fig. 1D). Results were consistent with adenocarcinomatous metastatic deposits. Immunohistochemistry was negative for ER, PR and HER-2 neu, and positive for cytokeratin 7, indicating breast as the primary site of neoplasm.

Hence, the patient was diagnosed as Zosteriform cutaneous metastasis and referred to the oncology department for further management.

Case 2

A 54-year-old female patient was referred from surgery OPD to dermatology OPD.

The patient reported the appearance of multiple painful nodules on the left side of the chest along with a mastectomy scar mark on the left side of the chest.

She was a known case of infiltrating ductal carcinoma breast, T4N2M0, and had undergone five cycles of neoadjuvant chemotherapy followed by salvage mastectomy 4 months ago.

On dermatological examination, the patient had a few grouped vesicles with crusted plaques and nodules with ulceration over the left mastectomy scar site and surrounding skin extending onto the left lateral side and back in dermatomal distribution along with reddish-yellow plaque with superimposed crusts and nodular surface with peau d' orange appearance on right side of chest (Fig. 2A and B).

Dermoscopy revealed multiple, discrete, polymorphic blood vessels with pinkish-white structureless areas and yellow areas (Fig. 2C).

Routine investigations were within normal limits.

Biopsy of the lesions was planned keeping Herpes zoster and zosteriform cutaneous metastasis as the two main differentials. HPE showed appearances consistent with metastatic carcinomatous deposits (Fig. 2D).

Immunohistochemistry was positive for ER, PR, cytokeratin 7, and negative for HER-2 neu, indicating breast as the primary site of neoplasm.

The patient was diagnosed as zosteriform cutaneous metastasis due to underlying malignancy and referred to the surgery department for further management.

Discussion

Breast cancer is the most common tumor associated with cutaneous metastasis (excluding melanoma) in clinical practice. The incidence of cutaneous metastasis in carcinoma breast is about 24%[8].

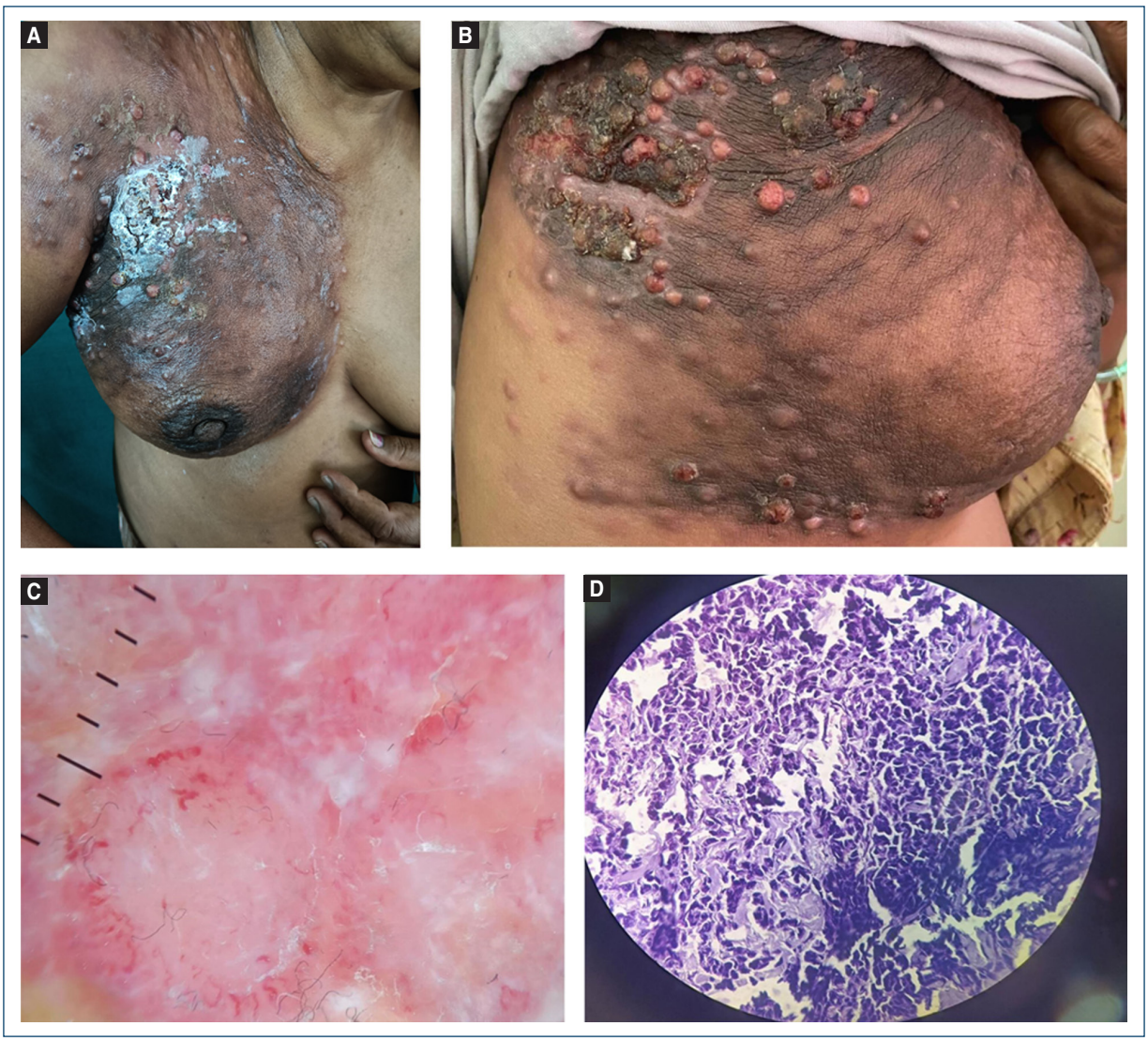

Figure 1. A: multiple crusted papulo-nodules with few vesicles on the right breast in a dermatomal distribution. **B:** close view of the lesions showing papulo-nodules in the same patient. **C:** ×10 magnification of DL4 dermoscope under polarized light: contact dermoscopy demonstrated yellow areas, polymorphic vessels, whitish bright lines, and structureless areas (depicted by black arrows). **D:** H&E ×40 showing dermal infiltration by hyperchromatic pleomorphic nuclei with increased nuclear: cytoplasmic ratio.

Various morphologies of breast carcinoma are seen, some of which are commonly encountered such as single to multiple erythematous infiltrating papules and nodules or ulcers. Other rare variants are carcinoma erysipeloides, carcinoma en cuirasses, carcinoma telangiectaticum, alopecia neoplastica, metastasis to the inframammary crease, and zosteriform metastasis (as in the abovementioned cases)[4]. Dermoscopy showing vascular structures within a cutaneous nodule in patients with known underlying cancer (as in our case reports) should raise suspicion for cutaneous metastasis as it suggests angiogenesis[9].

Histopathology of cutaneous breast carcinoma may show interstitial, nodular, mixed interstitial and nodular, or inflammatory carcinoma[10], while that of Herpes zoster shows multinucleated keratinocytes, acantholytic cells known as Tzanck cells with distinct nuclear inclusions, perineural infiltrate of lymphocytes and neutrophils, sometimes associated with intraneural involvement[11]. Biopsy, thus helps in confirming the diagnosis.

Treatment options of cutaneous metastasis include systemic chemotherapy, surgical resection, and radiation.

The prognosis of a patient with cutaneous metastasis depends primarily on the behavior of the underlying

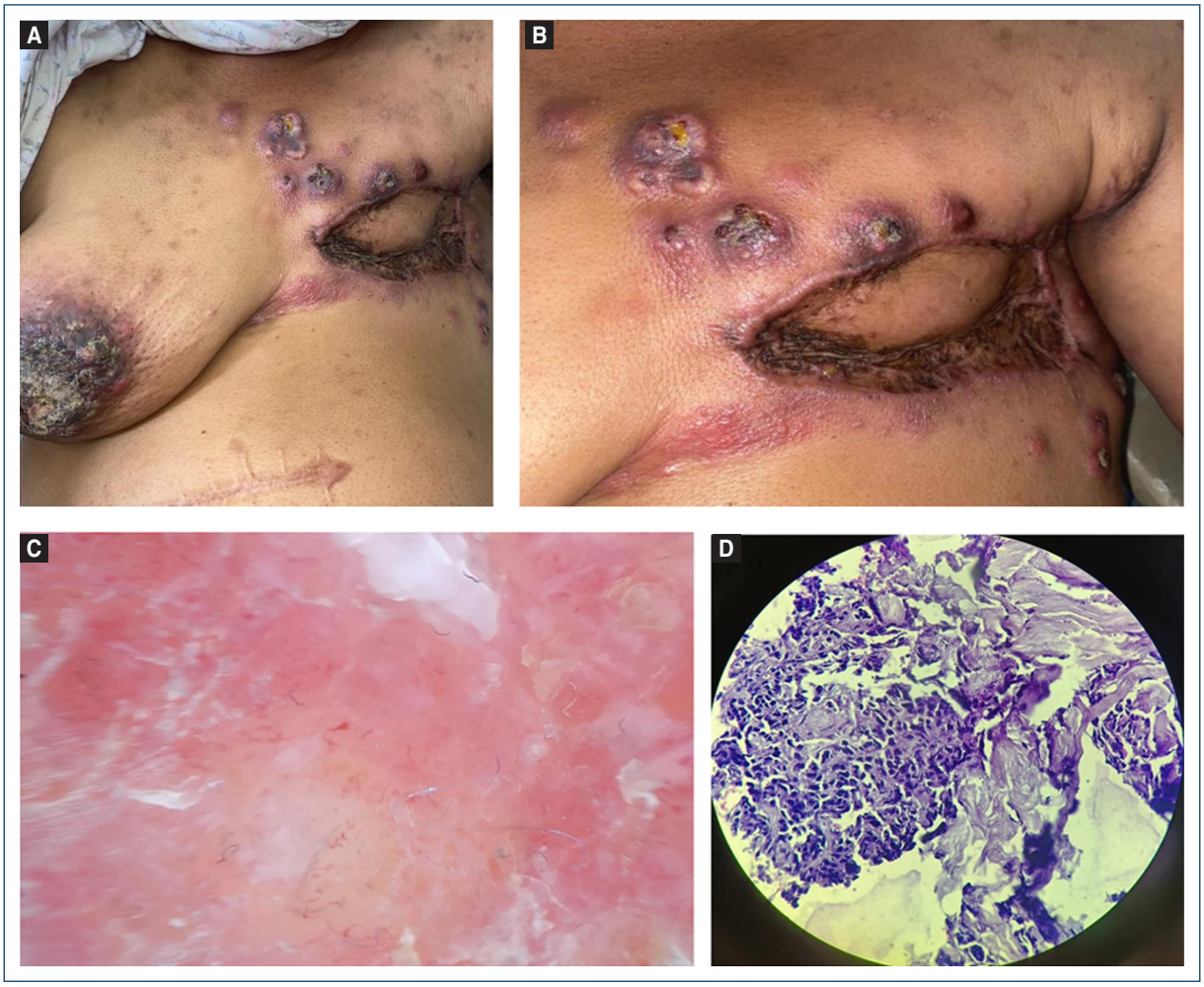

Figure 2. **A:** multiple grouped vesicles, papules, and nodules superimposed with crust on left breast in dermatomal distribution along with mastectomy scar. **B:** close view of the lesions showing the lesions in the same patient. **C:** ×10 magnification of DL4 dermoscope under polarized light: contact dermoscopy demonstrated multiple, discrete, polymorphic blood vessels with pinkish-white structureless areas and yellow areas (depicted by black arrows). **D:** H&E ×40 showing metastatic carcinomatous deposits.

tumor and its response to treatment. In breast carcinoma, immunohistochemistry plays a very important role in deciding the treatment and prognosis.

Cutaneous metastasis from breast cancer usually occurs in later stages[4]. However, if the underlying malignancy is not known, cutaneous metastasis can rarely present as the initial sign of the cancer. In either case, it shows poor response to treatment.

Conclusion

The above cases highlight the importance of differentiating herpes zoster from zosteriform cutaneous metastasis as it is a great mimicker of the former.

Since zosteriform metastasis is not so commonly seen, it is likely to be missed. In the elderly and cases of known underlying malignancy, zosteriform cutaneous metastasis should always be kept in mind though herpes zoster becomes the first differential due to the immunocompromising nature of the disease.

Biopsy is vital to confirm the diagnosis though dermoscopy aids in raising the suspicion.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

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Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

Punctate palmoplantar keratoderma type I: the clinical and genetic features of two family members with *AAGAB* gene mutation

Queratodermia palmoplantar punctata do tipo I: as características clínicas e genéticas de dois membros familiares com mutação do gene AAGAB

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Abstract

Hereditary punctate palmoplantar keratoderma type I (PPPK1) is a rare autosomal dominant disorder characterized by hyperkeratotic papules on the palms and soles, typically appearing in adolescence but occasionally manifesting later in life. We describe two family members, an African woman (61 years old) and her daughter (29 years old), presenting with multiple asymptomatic hyperkeratotic papules on the palms and soles. Histopathology revealed orthohyperkeratosis, acanthosis, hypergranulosis, and elongated rete ridges. Genetic analysis identified a heterozygous c.535+1G>A mutation in the *AAGAB* gene. Despite topical salicylic acid, urea, and tretinoin treatment, only minimal improvement was observed. PPPK1 pathogenesis involves genetic factors, with *AAGAB* being a major contributor, although other loci may be implicated. These cases highlight the phenotypic variability and delayed disease onset in some individuals, underscoring the need for further investigation into the underlying genetic mechanisms and effective treatment strategies.

Keywords: Punctate palmoplantar keratoderma. Hereditary keratodermas. *AAGAB* mutation.

Resumo

A queratodermia palmo-plantar punctata do tipo I (PPPK1) é uma doença autossómica dominante rara, caracterizada por pápulas hiperqueratósicas nas palmas e plantas, que geralmente surgem na adolescência, mas podem manifestar-se mais tarde na vida. Descrevemos dois membros de uma mesma família, uma mulher africana de 61 anos e a sua filha de 29 anos, ambas com múltiplas pápulas hiperqueratósicas assintomáticas nas palmas e plantas. A histopatologia revelou hiperqueratose ortoqueratósica, acantose, hipergranulose e cristas epidérmicas alongadas. A análise genética identificou uma mutação heterozigótica c.535+1G>A no gene *AAGAB*. Apesar do tratamento tópico com ácido salicílico, ureia e tretinoína, foi observada

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apenas uma melhoria mínima. A patogénese da PPPK1 envolve fatores genéticos, sendo o *AAGAB* um contributo importante, embora outros loci possam estar envolvidos. Estes casos destacam a variabilidade fenotípica e o início tardio da doença em alguns indivíduos, sublinhando a necessidade de mais estudos sobre os mecanismos genéticos subjacentes e estratégias de tratamento eficazes.

Palavras-chave: Queratodermia palmo-plantar punctata. Queratodermia hereditária. Mutação AAGAB.

Introduction

Hereditary palmoplantar keratodermas (PPK) are a heterogeneous group of rare skin disorders characterized by thickening of the epidermis of palms and soles[1]. PPK can be classified by the pattern of lesions into four clinical subtypes: diffuse, punctate, focal, and striate[1,2]. Isolated punctate PPK can be further subdivided into three variants: punctate PPK type 1 (Buschke-Fischer-Brauer disease), punctate porokeratosis (type 2), and acrokeratoelastoidosis (type 3)[3]. Herein, we describe the clinical and genetic features of two family members with punctate palmoplantar keratoderma type I.

Clinical case

A 61-year-old African woman presented with a 10-year history of multiple, small (0.3-1 cm), circular hyperkeratotic papules and plaques on the palms and soles (Figs. 1A and B). These skin abnormalities were asymptomatic and irregularly distributed. There were no additional complaints, such as keratoderma transgrediens, and no history of arsenic exposure, immunosuppression, or malignancy. Notably, her 29-year-old daughter also exhibited a similar dermatosis (Figs. 1C and D). A skin biopsy revealed marked orthohyperkeratosis overlying acanthotic epidermis with elongated and curved rete ridges (Fig. 2A) with prominent, coiled and dilated acrosyringia (Fig. 2B) and hypergranulosis, with no cytologic features of HPV infection (Fig. 2C). A computed tomography body scan ruled out malignancy. Based on the clinical and histological features, a diagnosis of type I hereditary punctate keratoderma was established. Genetic study of the *AAGAB* gene in both the mother and daughter identifies a heterozygous mutation in intron 5: *c.535+1G>A*. Subsequent mRNA analysis confirmed that the splicing mutation led to the deletion of exon 5, resulting in decreased protein levels. Notably, the mother reported that her sister and nephew had similar manifestations. As they both live abroad, they did not undergo genetic testing. The patients were treated with salicylic acid 30%, urea 40%, and tretinoin; however, only minimal clinical improvement was observed in both cases. Acitretin treatment was proposed to the mother, but the patient ultimately did not proceed with it. Over 5 years of follow-up, neither patient developed a history of neoplasia.

Discussion

Punctate palmoplantar keratoderma type I (PPPK1), first described in 1910, is a rare autosomal dominant inherited disorder characterized by multiple tiny punctate keratoses on the palms and soles[2]. Its estimated prevalence is approximately 1.17/100,000 individuals[4]. Lesions typically begin to develop in early adolescence but can also manifest later in life, as late as the fifth decade, as observed in our patient. PPPK1 is distinguished by numerous pinpoint, firm papules, 2-8 mm in diameter, which may progress to become translucent, opaque, or verrucous over time[4]. The papules gradually increase in number and size with age, and often coalesce in pressure-bearing areas of plantar skin[2]. The exact etiology of PPPK1 is not fully understood, but it is believed to involve a combination of genetic and environmental factors[3,4]. Several loci have been reported in the literature, with *AAGAB* being considered a major genetic factor[3]. This gene encodes the alpha- and gamma-adaptin binding protein, also known as p34. Mutations in this gene can increase epidermal growth factor receptor protein expression and tyrosine phosphorylation, resulting in cellular hyperproliferation[2,5]. To date, at least 50 different *AAGAB* mutations have been reported[1], including the *c.535+1G>A* mutation identified in our patient, which has been previously documented only once in a sporadic case within the Chinese population[6]. In addition, not all patients with a PPPK1 phenotype have an identified variant in *AAGAB*, suggesting the potential involvement of other, yet-to-be-identified causative genes[3]. Histological examination of PPPK1 typically reveals hyperkeratosis, unspecific changes such as acanthosis, parakeratosis (in some cases) and hypergranulosis. The dermis is usually normal and devoid of inflammatory infiltrate[4]. Clinically, PPPK1 can exhibit varying degrees of

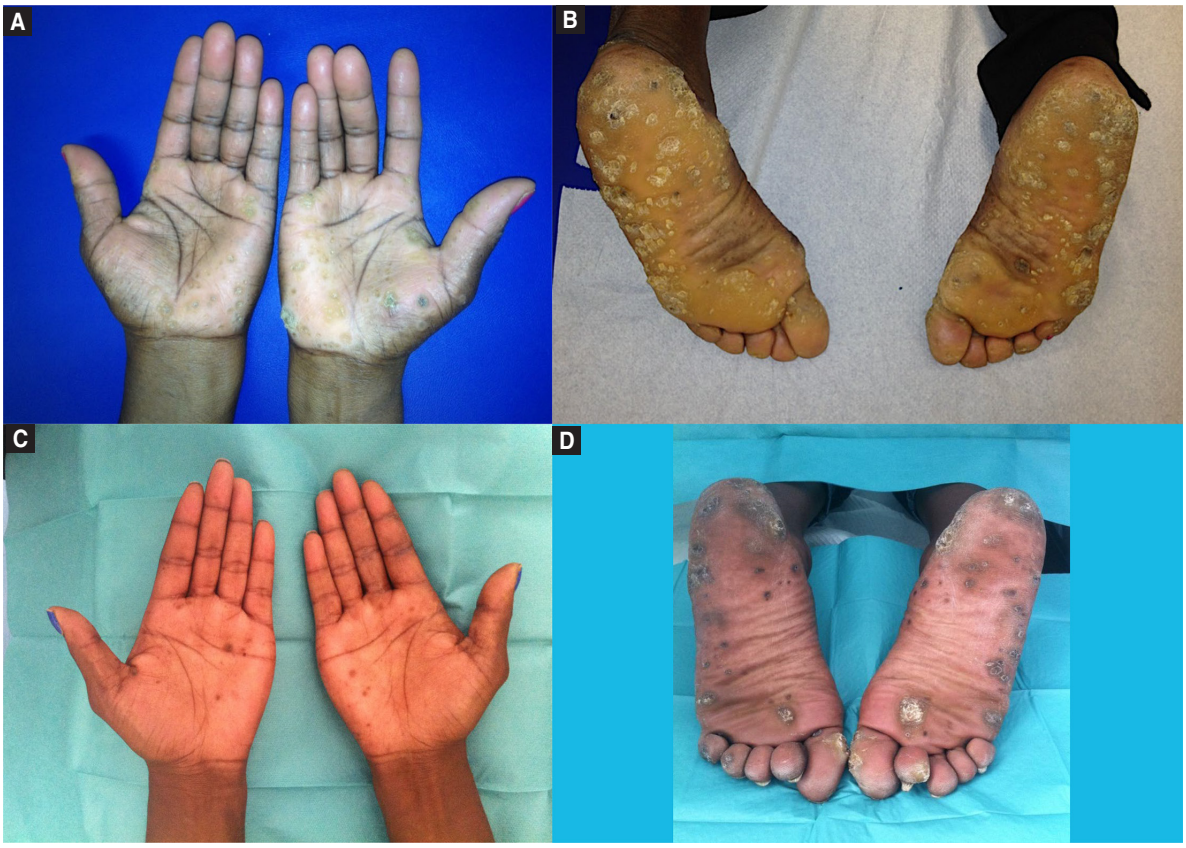

Figure 1. Clinical presentation: multiple small, circular hyperkeratotic papules and plaques on the palms and soles of both mother (**A** and **B**) and daughter (**C** and **D**).

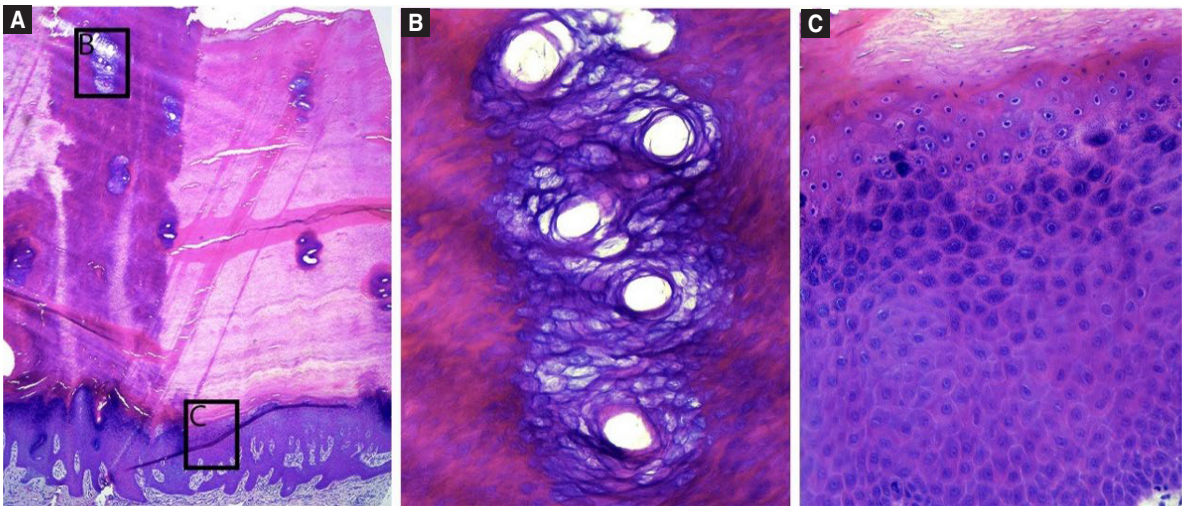

Figure 2. Histopathological examination: marked orthohyperkeratosis overlying acanthotic epidermis with elongated and curved rete ridges (**A,** H&E ×25); Prominent, coiled and dilated acrosyringium (**B,** H&E ×200); hypergranulosis with no cytologic features of HPV infection (**C,** H&E ×200).

severity between families, though the genotype-phenotype correlation remains poorly defined[2]. In the cases described, both the mother and daughter exhibited similar clinical severity, despite their symptoms starting 20 years apart. Although there have been reports suggesting an association between PPPK1 and malignancy, this link remains somewhat controversial[3]. Differential diagnoses to consider include verruca vulgaris, arsenic keratosis, punctate porokeratosis, acrokeratoelastoidosis, and focal acral hyperkeratosis[4]. The treatment for PPPK1 is primarily symptomatic, and typically involves topical keratolytics such as lactic acid, urea, and salicylic acid. Additional treatment options include phototherapy, systemic retinoids (such as acitretin and alitretinoin), and surgical interventions. These therapies generally lead to temporary reductions in skin thickness and improvement in skin softness[4].

Conclusion

This case report highlights the clinical, histological, and genetic findings of two family members with PPPK1. The clinical similarity between mother and daughter, despite differing ages of onset, illustrates the variable expressivity of the condition. Histopathological and genetic analyses played a key role in confirming the diagnosis. Continued research into the molecular mechanisms of PPPK1 is essential to idevelop more effective therapies.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

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Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

Cutaneous pathergy and squamous cell carcinoma: a report of two cases

Patergia cutânea e carcinoma espinocelular: relato de dois casos

Austinn C. Miller[1,2], Chinmoy Bhate[1,3], Monica Constantinescu[2,3], Julianna Gregory[3], and Armand B. Cognetta Jr.[1,2,3]*

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Abstract

Cutaneous pathergy is a phenomenon demonstrating an exaggerated wound response following minor trauma. While often associated with inflammatory conditions, its association with carcinogenesis is less often described. Recognition of this important phenomenon may be challenging to clinicians who do not encounter it regularly. Cutaneous pathergic squamous cell carcinomas (SCCs) most typically occur as numerous eruptive neoplasms in female patients in sites of trauma or in the background of lichen simplex chronicus or lichenoid dermatoses. Management can be difficult and is typically non-surgical. Herein, we describe two cases of pathergic SCCs and our approach to treatment.

Keywords: Pathergy. Cutaneous squamous cell carcinoma. Fluorouracil. Retinoid.

Resumo

A patergia cutânea é um fenômeno que demonstra uma resposta exagerada da ferida após pequenos traumas. Embora frequentemente associada a condições inflamatórias, a sua associação com a carcinogénese é menos frequentemente descrita. O reconhecimento deste importante fenómeno pode ser um desafio para os médicos que não o encontram regularmente. Os carcinomas cutâneos de células escamosas patérgicas ocorrem mais tipicamente como numerosas neoplasias eruptivas em pacientes do sexo feminino em locais de trauma ou no contexto de líquen simples crônico ou dermatoses liquenoides. O manejo pode ser difícil e normalmente não é cirúrgico. Aqui, descrevemos dois casos de carcinoma espinocelular patérgico e nossa abordagem ao tratamento.

Palavras-chave: Patergia. Carcinoma espinocelular cutâneo. Fluorouracil. Retinóide.

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Introduction

Cutaneous pathergy is a phenomenon demonstrating an exaggerated wound response following minor trauma. While often associated with inflammatory conditions such as Bechet's disease and pyoderma gangrenosum, carcinogenesis secondary to pathergy has been described[1-3]. We have previously described cutaneous eruptive post-operative squamous cell carcinomas (SCCs) exhibiting a pathergy-like reaction around surgical wound sites[1]. The pathogenesis for this process is not well understood. We have noted it to occur more frequently on the lower extremities. Recognition of this phenomenon may be perplexing to clinicians who do not encounter it regularly; it may represent a practice gap for plastic surgeons and dermatologists who perform cutaneous surgery. Herein, we report on two female patients with a multitude of pathergic SCCs demonstrating a dramatic response to our therapeutic regimen.

Report of two cases

Case 1

A 67-year-old woman presented with a 6-month history of > 50 erythematous plaques/nodules on her bilateral pre-tibial skin (Fig. 1A). The patient did not have any predisposing medical history or risk factors aside from having type II Fitzpatrick skin type. The lesions were tender and intensely pruritic. Concerning nodules were biopsied, with most demonstrating well-differentiated SCCs and others lichen simplex chronicus. The patient was diagnosed with pathergic SCCs. She was treated with our standard regimen of oral acitretin, 25 mg, 5 days/week, 0.1-0.5 mLs of 50 mg/mL intralesional fluorouracil weekly to biopsy-proven SCC, and 10-40 mg of intramuscular triamcinolone monthly. Lichen simplex chronicus was treated with triamcinolone 0.1% cream under occlusion and intralesional-triamcinolone. The patient was followed weekly until all SCCs resolved then transitioned to monthly visits. Acetretin was weaned to 10 mg with the goal of stopping once the patient remained cancer-free for 12 months. The patient tolerated the treatment regimen without side effects or signs of toxicity. At 8 months, only two stable non-malignant lichen simplex chronicus nodules remained (Fig. 1B).

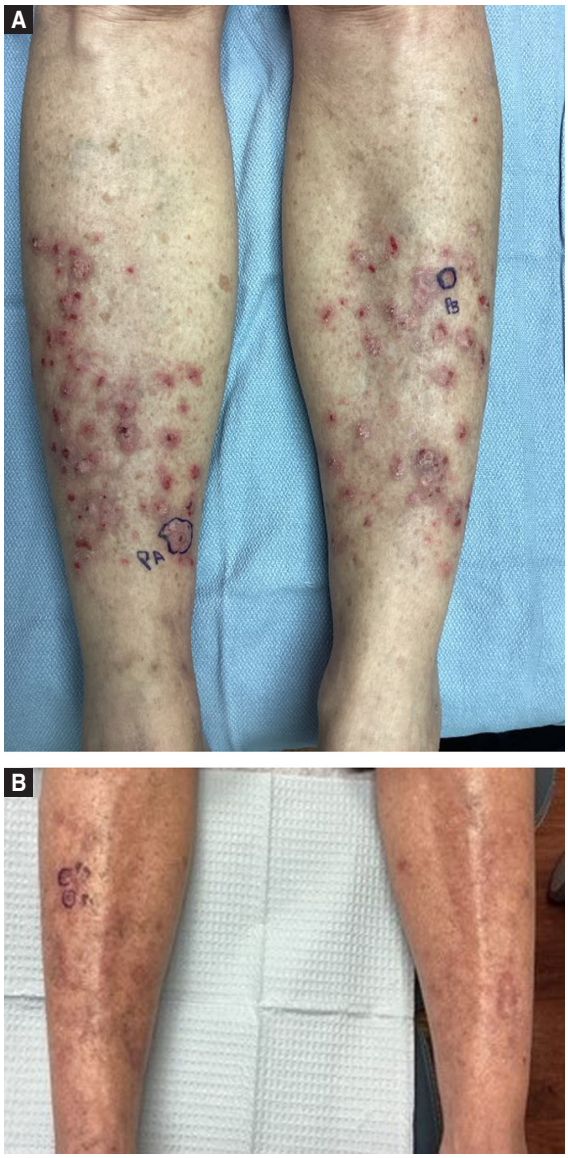

Figure 1. A: at presentation, numerous erythematous-violaceous plaques and nodules with overlying excoriations appear on the bilateral pre-tibial areas. **B:** at 8 months, two small, stable lichen simplex chronicus remain.

Case 2

A 72-year-old woman presented with numerous erythematous keratotic nodules on her bilateral pre-tibial skin. She endorsed frequent trauma to this area. Concerning lesions were biopsied, all consistent with SCCs. The patient did not have any predisposing medical history or risk factors aside from having type II Fitzpatrick skin type. The patient was placed on a

similar follow-up and treatment regimen of acitretin, intralesional fluorouracil, and intramuscular triamcinolone. Over the course of 3 years, 20 SCCs were treated with this regimen. The patient improved and remained SCC-free for 12 months prompting discontinuation of treatment. Within a month of stopping, the patient developed new lesions. An invasive SCC formed in the scar of a previous intralesional fluorouracil site. Mohs surgery was performed with negative margins (Fig. 2A). Two months afterward, the patient had prompt development of three new SCCs adjacent to the scar (Fig. 2B). The treatment regimen of intralesional fluorouracil was restarted with good response.

Discussion

The exact pathogenesis of pathergic SCCs remains unclear. Studies of pathergy favor an immune-mediated T-cell reaction, similar to a delayed-type hypersensitivity reaction, initiated through mechanically damaged epidermal and dermal components[1,4]. The reaction may vary depending on the involved condition, the type/severity of trauma, and ethnicity[4].

Patients often describe chronic itching and recurrent trauma, including surgery. Pathologic changes may be initiated or exacerbated by external stimuli along with immune dysregulation, increased cell turnover, and microenvironment changes in the setting of chronic inflammation. The use of systemic steroid therapy in our treatment regimen stems from this intrinsic autoinflammatory hypothesis. Moreover, SCCs has been observed to develop within other inflammatory disorders of the skin, including psoriasis, lichen planus, lichen simplex chronicus, herpes virus infections, and chronic wounds (Wolf's isotopic response)[5]. The pathway to malignant transformation in these conditions is poorly understood[6].

Treatment of benign pathergy-induced conditions is typically predicated on avoidance of additional skin trauma and amelioration of pruritus. Systemic, intralesional, and topical steroids are vital in halting the itch-scratch cycle seen with concomitant conditions such as lichen simplex chronicus/prurigo nodularis. The management of cutaneous malignancies, including SCCs, in this context, may pose a conundrum because traditional excision may not be suitable. In addition, patients in this setting often manifest with many lesions in poorly-perfused anatomic sites of the lower extremities[6]. Once pathergy is recognized, the non-surgical intervention appears to provide the best response in our experience. Besides intralesional injections of fluorouracil or methotrexate, many regimens also include systemic retinoids such as acitretin or isotretinoin. The rationale for the latter is that retinoids are known to affect epidermal turnover and keratinization.

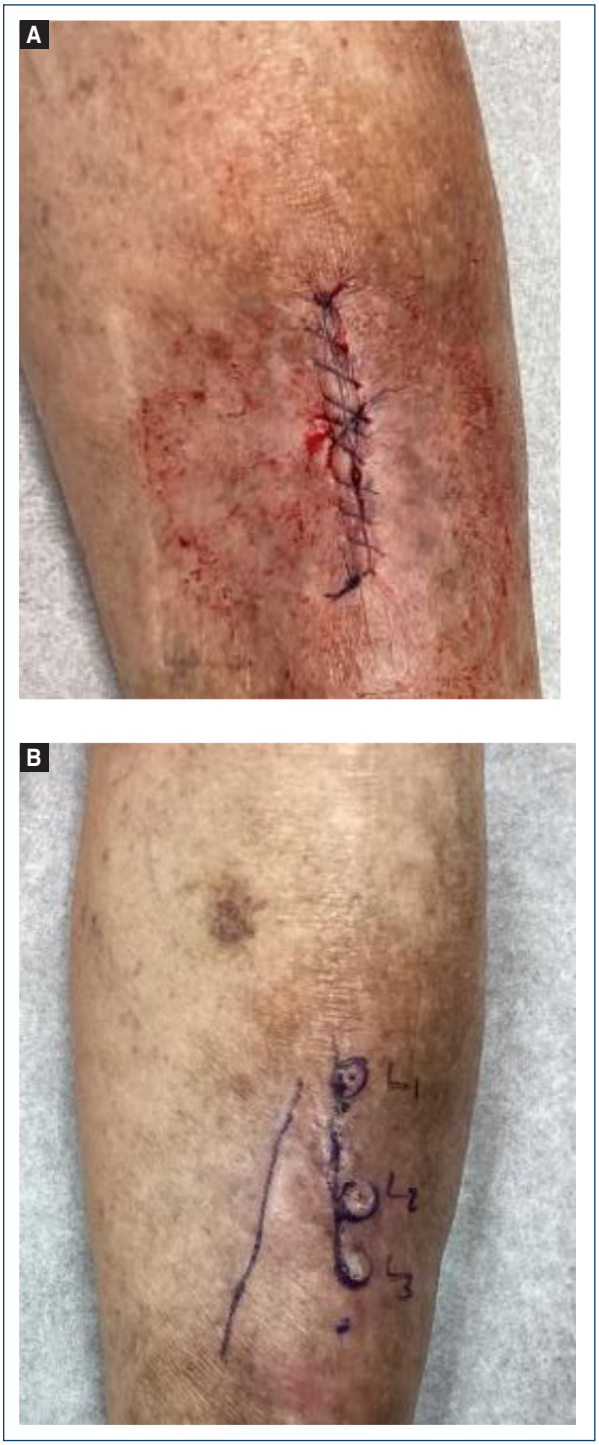

Figure 2. A: linear repair status post-Mohs surgery with clear margins. **B:** pathergic squamous cell carcinomas occurring 2 months following Mohs surgery.

It is for this reason that they have also historically been used to manage psoriasis, another condition in which inflammatory, non-malignant, epidermal proliferation and pathergy occurs[1-3]. Aggressive combination therapy and close follow-up are necessary to properly manage this challenging clinical scenario.

Conclusion

Cutaneous pathergy represents a rare but significant mechanism in the development and propagation of eruptive squamous cell carcinomas, particularly in predisposed individuals with chronic inflammatory skin conditions or repeated trauma. The two cases presented underscore the diagnostic and therapeutic complexities of managing pathergy-associated SCCs, especially when arising on the lower extremities. Our experience highlights the utility of a nonsurgical, multimodal regimen combining systemic retinoids, intralesional chemotherapy, and corticosteroids to effectively control disease activity, reduce lesion burden, and manage underlying inflammatory triggers. Early recognition of this phenomenon is essential to avoid unnecessary surgical interventions, which may exacerbate the condition. As pathergic SCC remains an under-recognized entity, greater awareness and interdisciplinary collaboration between dermatologists, surgeons, and oncologists are crucial for optimizing patient outcomes in this challenging and often recurrent disease process.

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Conflicts of interest

The views expressed in this publication represent those of the authors and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

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Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

Unveiling the mystique: pseudoxanthoma elasticum case report

Revelando o mistério: relato de caso de pseudoxantoma elástico

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Abstract

Pseudoxanthoma elasticum (PXE) is a rare genetic disorder of autosomal recessive inheritance affecting the skin, eyes, and cardiovascular system. We report a case of 17-year-old female with well-defined reticulated, skin-colored plaques over the anterior aspect and in nape of the neck. Punch biopsy from the lesion revealed benign stratified squamous lining with the middle and lower thirds of the dermis showing fragmented and calcified basophilic elastic fibers amidst collagen bundles. Adjacent areas show dense lymphocytic infiltration and giant cell reaction. Verhoff Von Gieson stains showed black-colored fragmented elastic fibers. Ocular examination revealed peau d' orange appearance of retinal blood vessels, which was considered as the early stage of retinal involvement. PXE is currently an incurable disease that on early diagnosis can prevent the Ocular and cardiovascular complications.

Keywords: Autosomal recessive. Elastic fibers. Pseudoxanthoma elasticum.

Resumo

Pseudoxantoma elástico é uma doença genética rara de herança autossômica recessiva que afeta a pele, os olhos e o sistema cardiovascular. Relatamos o caso de uma mulher de 17 anos com placas reticuladas bem definidas, da cor da pele, na área do decote e na nuca. A biópsia por punção da lesão revelou revestimento escamoso estratificado benigno com terços médio e inferior da derme mostrando fibras elásticas basofílicas fragmentadas e calcificadas em meio a feixes de colágeno. A área adjacente mostra infiltração linfocítica densa e reação de células gigantes. A coloração de Verhoff Von Gieson mostrou fibras elásticas fragmentadas de cor preta. O exame ocular revelou aparência de vasos sanguíneos da retina em tons de laranja e peau-d, o que foi considerado o estágio inicial do envolvimento da retina. O PXE é atualmente uma doença incurável que, no diagnóstico precoce, pode prevenir complicações oculares e cardiovasculares.

Palavras-chave: Autossômica recessiva. Fibras elásticas. Pseudoxantoma elástico.

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Introduction

Pseudoxanthoma elasticum (PXE) is a rare genetic disorder with an autosomal recessive mode of genetic transmission affecting multiple organs, such as the skin, eyes, heart, and gastrointestinal system[1]. PXE, also termed as Gronblad Strandberg syndrome, is a rare disorder due to a mutation in the *ABCC6* gene (ATP-binding cassette transporter C6), located in chromosome 16. Prevalence of PXE was found to be 1/25.000 to 1/100.000 inhabitants. It has been found that the prevalence of PXE is 10 times more in women than in men[2,3]. It encodes an ATP-binding driven anion transporter, seen in the cell membrane of the liver and kidney. PXE is a form of genodermatoses, currently an incurable disease associated with serious complications due to elastic fiber fragmentation and calcification[4]. Here we report a rare case of PXE with its clinical, histopathological, and ocular findings.

Case report

A 17-years-old female came to the outpatient department with the complaints of itchy, yellowish papules and plaques in the anterior and lateral aspect of her neck for the past 1 year. No relevant personal or family, or any medical history of dermatosis. No history of any consanguineous marriage in the family. On examination, painless, uneven skin-colored reticulated plaques (Fig. 1) without any surrounding inflammatory signs were seen in the anterior aspect and in the nape of the neck, giving a parchment-like skin appearance.

Complete hemogram and routine blood investigations were found to be normal. The patient was then subjected to a skin biopsy. A punch biopsy was taken from the lesion in the anterior and nape of the neck. Biopsy revealed benign stratified squamous lining with middle and lower thirds of dermis showing fragmented and calcified basophilic elastic fibers amidst collagen bundles. The adjacent area shows dense lymphocytic infiltration and giant cell reaction (Fig. 2).

Verhoff Von Gieson stains showed black-colored fragmented elastic fibers in the dermis (Fig. 3).

Diagnosed as a case of PXE and the patient was then subjected to ocular examination, which revealed peau d' orange appearance of retinal blood vessels, which was the earliest retinal manifestation. Following the investigation, the patient was then subjected to cardiovascular evaluation and the results were normal. The patient is currently on follow-up.

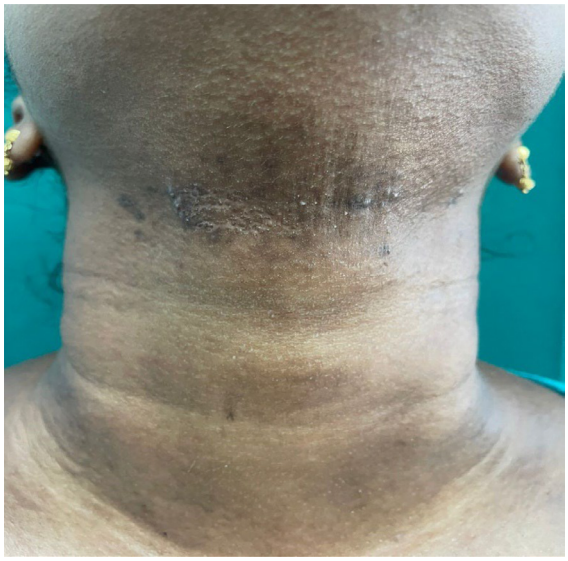

Figure 1. Clinical image of patient showing reticulated plaques over the anterior aspect of the neck.

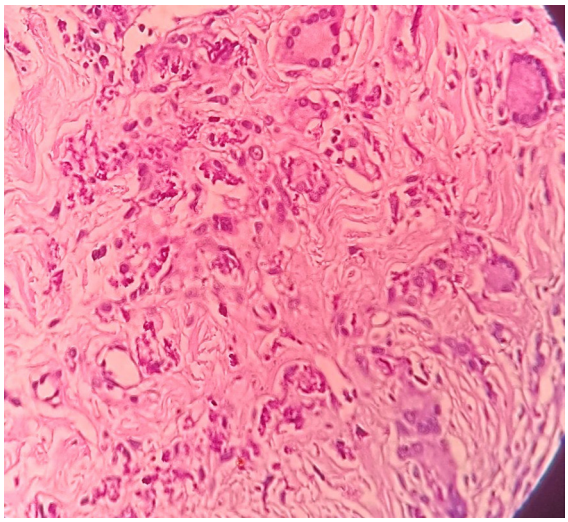

Figure 2. Histopathological image showing fragmented elastic fibers with calcification, lymphocytic infiltration, and giant cell reaction (H&E stain, 40×).

Discussion

PXE is a rare inherited genetic disorder, caused due to abnormal mineralization of the connective tissue with elastic fibre degeneration affecting various organs, such as the skin, eyeballs, and cardiovascular system[5].

Cutaneous manifestations are seen as yellowish macules or papules, or plaques. PXE can occur at any age

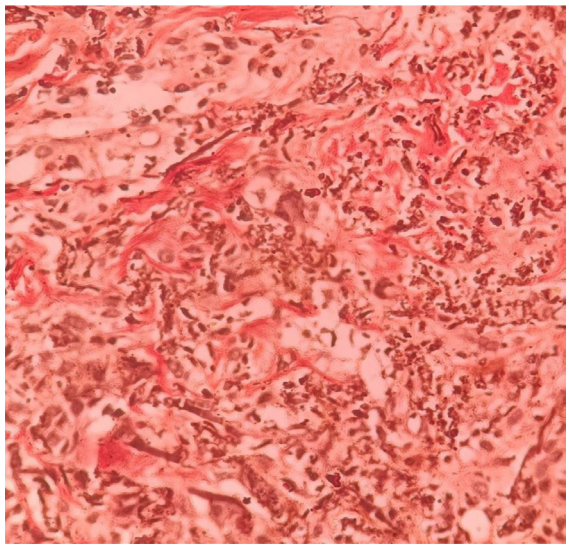

Figure 3. Histopathological image showing fragmented elastic fibers (Verhoeff Von Gieson stain, 40×).

and the skin appears lax and wrinkled. The lesions start appearing over the lateral aspects of the neck, followed by skin creases, armpits, popliteal, and inguinal regions. Oral mucosa and genital region can also be affected[6,7].

Early ocular involvement starts as peau d' orange appearance of retinal vessels and progresses to the development of angioid streaks due to lesions over the Bruch membrane. Progressive retinal pigmentation, macular degeneration, choroidal neovascularization, retinal hemorrhage, and scar formation can occur, leading to the most serious complication of complete ocular blindness[8].

Various cardiovascular abnormalities occur in a case of PXE, such as bradycardia, hypertension, angina pectoris, atherosclerosis, and cardiac arrest at younger ages. Gastrointestinal manifestations, including melena, hemorrhages, and hematemesis, can be seen. Some patients presented with stroke at younger ages. Major pathogenesis behind these complications was found to be fragmentation of elastic fibers in the lining of blood vessels and in the connective tissue of the pericardium, myocardium, and endocardium of the heart[9].

Certain inherited hemolytic disorders, such as beta thalassemia, hereditary spherocytosis, and Sickle cell anemia, can occur in patients with PXE[10].

Plomp et al. proposed guidelines for diagnosing PXE which includes major criteria: (a) skin lesions, such as yellow cutaneous plaques and papules, fragmentation, clumping, and calcification of elastic fibers, (b) ophthalmic lesions, such as Peau d' orange appearance of retina or the presence of angioid streaks, and (c) genetic factors such as mutation of both alleles of *ABCC6* gene or a first degree relative affected with PXE. Minor criteria include ophthalmic lesions, such as one angioid streak shorter than 1 disk diameter, one or more comets in the retina, and one or more wing signs in the retina: genetic factors, such as the presence of a mutation of one allele of the *ABCC6* gene[11].

Major differential diagnosis for PXE includes solar elastosis, PXE-like papillary dermal elastolysis. PXE-like papillary dermal elastolysis occurs in elderly females, where partial or complete loss of elastic fibers were seen but without calcification. Solar elastosis shows irregularly thickened, coarse, disorganized, and tangled elastic fibers[12].

Conclusion

This case report deals with a young female with typical clinical and histopathological features of PXE highlighting a need for a multidisciplinary approach for accurate diagnosis of this rare disorder. This helps us to understand the disease better and to discover the newer therapeutic approach to treat the disease and to prevent the complications as early as possible.

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Conflicts of interest

None

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the Institutional Ethics Committee.

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DERMATOLOGY IMAGES

Digital ulcers as a manifestation of a severe variant of carpal tunnel syndrome

Úlceras digitais como manifestação de uma variante grave da síndrome do túnel do carpo

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A 67-year-old woman presented to the dermatology department with a 6-month history of paresthesia and painless unilateral skin ulceration on the second fingertip of the right hand, with an adjacent distal violaceous macule. In the third fingertip a distal brownish macule with small vesicles was observed (Fig. 1). Laboratory studies, including antinuclear antibody testing, showed no abnormalities. Hand radiograph revealed diffuse osteopenia, without osteolysis, and electromyography showed severe sensory-motor stage compression of

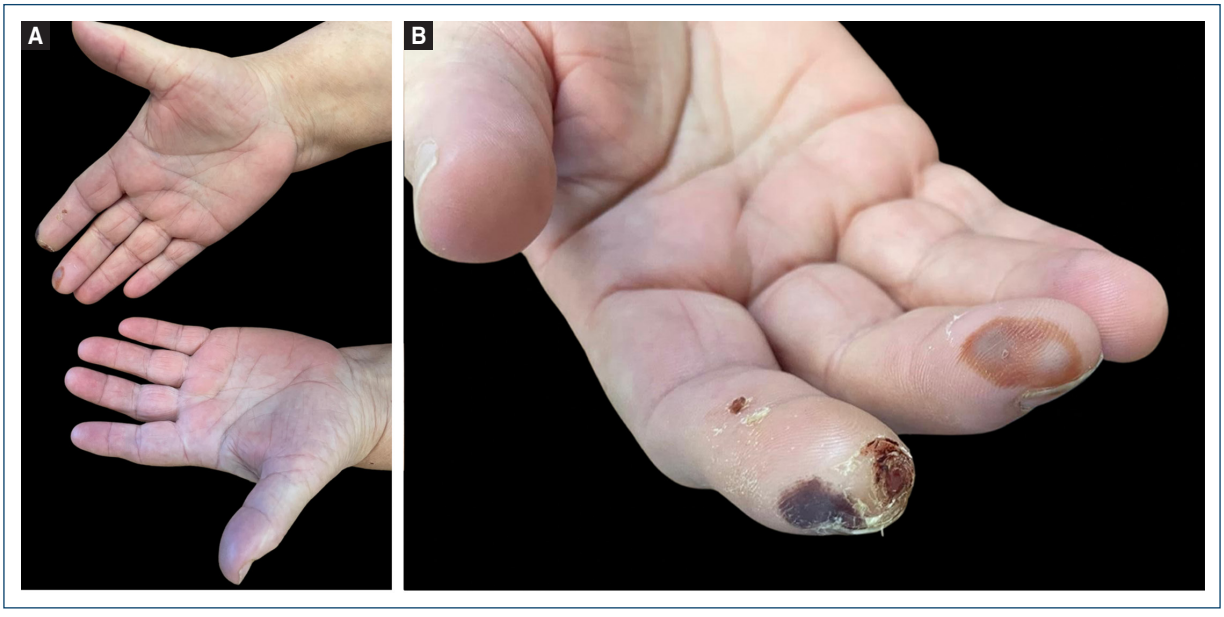

Figure 1. Skin ulceration on the second fingertip of the right hand, with an adjacent distal violaceous macule suggestive of subcorneal hemorrhage and a small erosion covered with crust in the second phalange. In the third fingertip, a distal brownish macule with small vesicles is shown **(A** and **B)**.

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the median nerve. The diagnosis of ulcerating carpal tunnel syndrome (CTS) was established and the patient was referred for orthopedic surgical treatment, showing significant improvement at 1-year follow-up.

This rare form of CTS arises from longstanding median nerve compression, leading to autonomic dysfunction, which is thought to contribute to the development of ischemic cutaneous changes in the digits[1]. Such cutaneous findings are otherwise uncommon in classical CTS[2]. Cutaneous lesions initially present with erythema, edema and bullae, eventually leading to unilateral painless ulcers on the palmar surface of the second and third fingertips[3–5]. Nail abnormalities like hyperkeratosis and onycholysis can also be present, although they were not observed in our patient[2]. Diagnosis is based on clinical assessment, supported by hand radiographs and electrophysiological tests, which can demonstrate median nerve dysfunction. Patients are often misdiagnosed with systemic sclerosis or Raynaud disease and autoantibody tests should be conducted[3]. Carpal tunnel release surgery remains the most effective treatment, as it resolves nail and skin lesions and prevents irreversible changes like acro-osteolysis[2–4].

This entity should be considered in the diagnosis of patients with unilateral ulcerations and nail changes limited to the second and third fingers, accompanied by sensory and motor changes along the median nerve pathway.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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DERMATOLOGY IMAGES

Lobomycosis with atypical morphology and location

Lobomicose de morfologia e localização atípicas

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A 44-year-old female patient, from Tapauá, Amazonas, was observed with a scaly nodular plaque with an irregular erythematous-brownish surface and meliceric crusts, extending over the entire lower region of the left buttock. It was present since she was 19 years old (Fig. 1).

The histopathological revealed skin with proliferative connective tissue in the dermis, accompanied by an inflammatory infiltrate composed of histiocytes, lymphocytes, and numerous giant cells, with numerous rounded fungal structures observed (Fig. 2).

Lobomycosis is a rare chronic granulomatous mycosis caused by the fungus *Lacazia loboi*, which has not been cultured in the laboratory yet. The infection occurs through traumatic inoculation of the fungus into the skin, with an incubation period of 1-2 years. Clinically, it manifests as keloid-like nodular lesions that evolve insidiously, most commonly in exposed areas[1,2]. It is endemic in tropical regions, with a greater concentration in the Amazon region, especially in Acre, and among male rural workers. The diagnosis is confirmed by histopathological examination or direct microscopy, which reveals characteristic fungal structures. Although rare, there is a risk of progression to squamous cell carcinoma in chronic lesions[3,4].

We describe a case of lobomycosis, characterized by significant particularities, including the atypical morphology of the lesions with a satisfactory therapeutic response to itraconazole 100 mg every 12 h for 1 year and 6 months. After treatment, only atrophic scars remained (Fig. 3), with no need for surgical interventions or combined treatments, which is an uncommon in this disease.

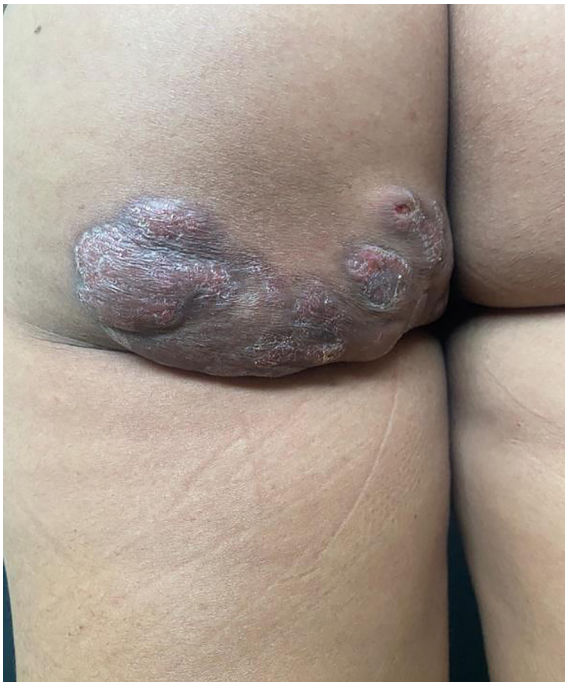

Figure 1. Skin lesion before treatment.

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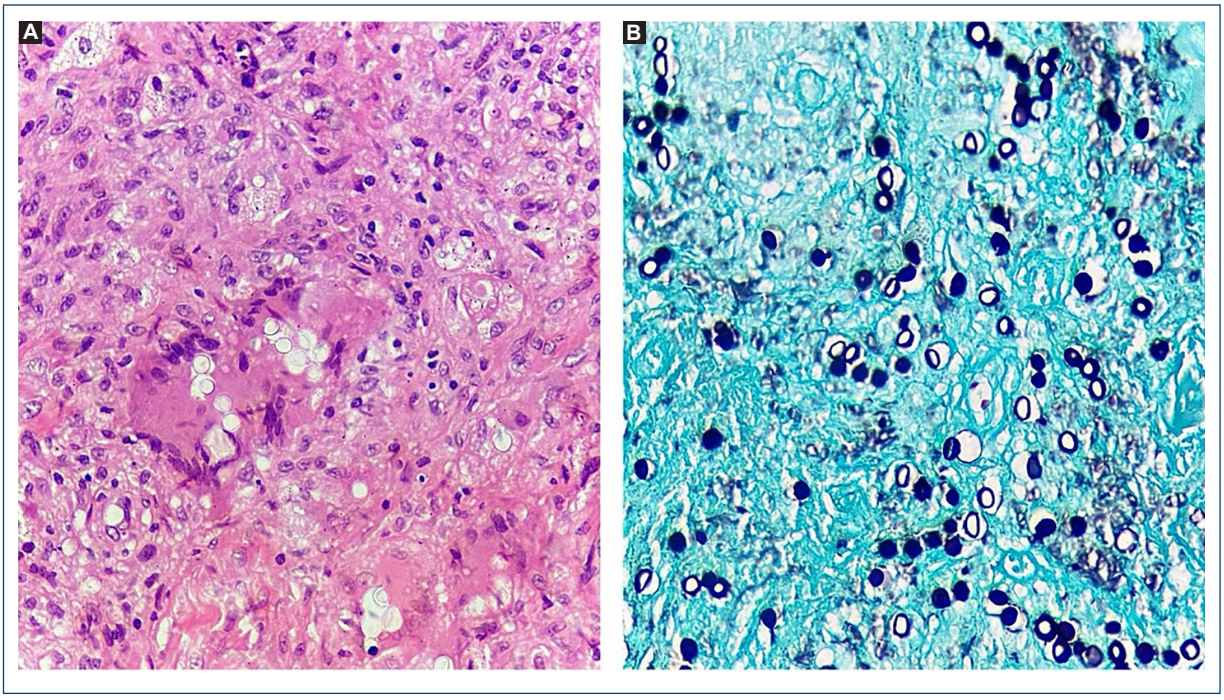

Figure 2. A: the sections show skin with dermal proliferation of connective tissue along with inflammatory infiltrate composed of histiocytes, lymphocytes, and numerous giant cells. Numerous rounded fungal structures are observed. (hematoxylin and eosin (H&E), x400). **B:** numerous fungal structures are observed (Grocott-Gomori, x400).

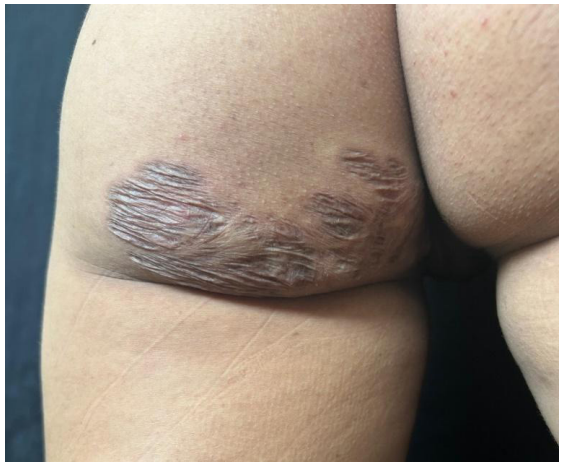

Figure 3. Atrophic scars after treatment.

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Conflicts of interest

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Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

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Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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DERMATOLOGY IMAGES

Exuberant cutaneous manifestation of secondary syphilis in a patient with human immunodeficiency virus infection

Sífilis secundária exuberante em paciente infectado pelo vírus da imunodeficiência humana

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A 40-year-old man, diagnosed with human immunodeficiency virus (HIV) infection reported lesions on his face for 6 months, without other symptoms. The patient was under antiretroviral therapy (HAART), with an undetectable viral load and CD4 T lymphocytes of 348 cel/mm^3. On physical examination, infiltrated violaceous plaques were observed on the face, distributed mainly on the forehead and temporal regions. Perioral lesions had an annular and circinate configuration, with scaly edges. Erythematous-scaly plaques were observed on the trunk and legs (Figs. 1 and 2). Laboratory screening revealed a positive venereal disease research laboratory (VDRL) (1:512) and numerous plasma cells were observed in skin biopsy, confirming the diagnosis of secondary syphilis. Treatment was performed with 3 weekly doses of benzathine penicillin, with total resolution of the lesions, no scarring sequelae on the skin and improvement in laboratory tests. Treponemal tests were not performed due to difficulties in patient adherence. Nevertheless, characteristics of skin biopsy and the response to therapy were considered sufficient to confirm the diagnosis.

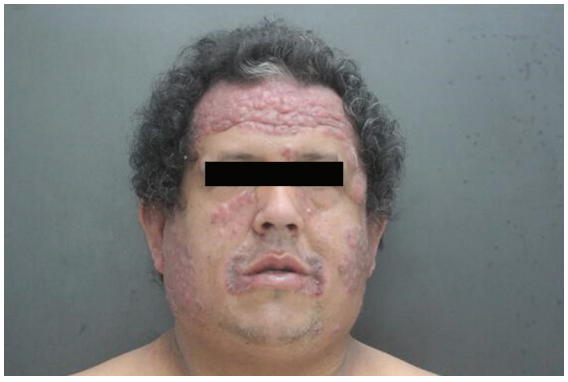

Figure 1. Infiltrated and confluent erythematous-violaceous plaques on the face, mainly affecting the forehead and temporal and perioral regions.

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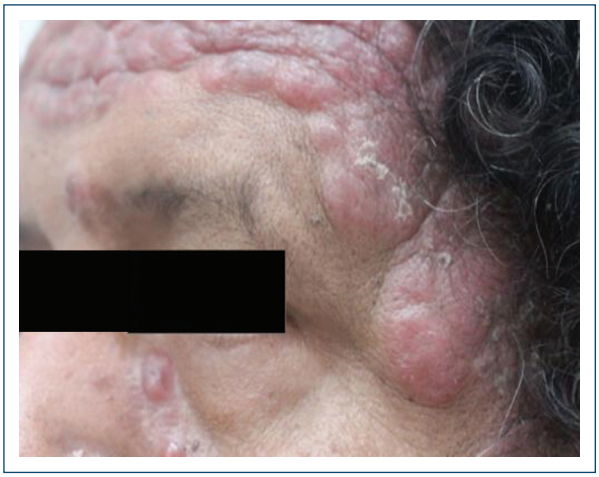

Figure 2. Infiltrated erythematous-violaceous plaque, with slight scaling in temporal region.

Long description

Syphilis and HIV are public health problems of global scope and a unique synergy between the two diseases has been described[1]. Infection by *Treponema pallidum* can increase the viral load and decrease the number of CD4+ T lymphocytes. Syphilis progression usually occurs in a predictable manner in immunocompetent patients; however, in the case of patients co-infected with HIV, prolonged and severe cutaneous manifestations, as well as atypical forms, are described[2,3]. This case highlights the importance of suspecting atypical forms of syphilis in HIV-infected patients, even with well-controlled disease and good adherence to HAART.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

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LETTER TO THE EDITOR

Intralesional corticosteroids: an overview of availability, dilution, and standardization across dermatological practices in Portugal

Corticosteroides intralesionais: uma visão geral da disponibilidade, diluição e padronização nas práticas dermatológicas em Portugal

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Dear Editor,

Intralesional corticosteroids (ILCS) are commonly used in dermatology as one of the primary therapeutic options for numerous conditions, including keloids, hypertrophic scars, alopecia areata, and inflammatory dermatoses, among others[1]. Their ability to deliver high concentrations of corticosteroids directly to the lesion, while minimizing systemic exposure, has contributed to their popularity. Diseases for which ILCS are particularly valuable are extensive, making these treatments indispensable for dermatologists[1].

One of the most critical aspects of administering ILCS is the proper dilution of the drug[2,3]. The potency of ILCS can lead to complications if not administered correctly, especially in sensitive areas such as the face, where the skin is thin. The most common side effects of improperly diluted corticosteroids include cutaneous atrophy, pigmentary changes, vascular complications and, in rare cases, systemic absorption leading to adrenal suppression[2-6].

Cutaneous atrophy is particularly concerning in long-term use, as it results in the thinning of the skin and subcutaneous tissues, creating a visible depression or even ulceration at the injection site. In addition, telangiectasias and purpura may occur. Pigmentary changes are also frequently observed, with either hyperpigmentation or hypopigmentation occurring, depending on the individual's skin type. These side effects are often dose-dependent, further underscoring the importance of correct dilution[2-6].

Unfortunately, the availability of different types of ILCS varies greatly across countries. In some regions, there are only a few options available, which may limit treatment choices for dermatologists. Triamcinolone acetonide (e.g., Trigon Depot®), accessible in countries such as Spain[5] and the United States, is the most widely studied corticosteroid for intralesional use; however, it is not commercialized in Portugal, being only available by an Especial Authorization Procedure (an importation procedure) given by the Portugal National Health Authority, INFARMED.

Available corticosteroids with licensed intralesional usage in Portugal are methylprednisolone acetate (Depo-Medrol®), dexamethasone sodium phosphate (Dexametasona Pharmakern®), and Diprofos Depot®. The latter is likely the most frequently used alternative in clinical practice according to authors' experience. It is provided in 14 mg/ 2mL vials, which includes both a fast-acting component (betamethasone sodium phosphate) and a long-acting component (betamethasone dipropionate). The dual-phase release mechanism makes Diprofos Depot® effective for both immediate and sustained anti-inflammatory action[6].

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Table 1. Equipotent concentrations of triamcinolone acetonide and betamethasone base

Corticosteroid	Equipotent concentration (mg)
Triamcinolone acetonide	4.4
Betamethasone base	0.75

Table 2. Equipotent concentrations and appropriate dilutions of ILCS

Triamcinolone acetonide (mg/mL)	Betamethasone (mg)*	CS (mL)†	NS 0.9% (mL)†	Dilution (CS:NS)
40	7	1	0	1:0
20	3.50	0.50	0.50	1:1
10	1.75	0.25	0.75	1:3
5	0.88	0.12	0.88	1:7
2.5	0.44	0.06	0.94	1:15

*Using 5.87 × (= 4.4/0.75) as equipotent conversion rule.
†Minor adjustments to volumes were made to respect syringe accuracy of two decimals (ex. insulin syringe of 1 mL).
Dilutions should be done according to drug label with normal saline (NS) 0.9% or lidocaine 1-2%. To simplify calculations while minimizing clinical impact, 6.8 was regarded as 7 mg of betamethasone. Calculations were made to a final volume of 1 mL. For higher volumes, the following values should be multiplied accordingly.
CS: corticosteroid; NS: normal saline; ILCS: intralesional corticosteroids.

A common challenge for clinicians is the lack of standardized guidelines on dilution for different types of corticosteroids. Understanding how to convert between different corticosteroids is essential due to variations in their availability and potency. This knowledge can help avoid overtreatment or undertreatment, both of which may compromise clinical outcomes.

To assist clinicians in standardizing the use of ILCS, the following table provides equipotent conversion data from triamcinolone acetonide to betamethasone (Tables 1 and 2). These tables offer practical guidance for ensuring that patients receive an equivalent therapeutic dose, regardless of which corticosteroid of the two is used.

Additional considerations are also important to ensure optimal outcomes, such as preparing the dose immediately before injection and gently shaking or rolling the syringe beforehand to ensure the drug is evenly suspended. It is also recommended to use a maximum of 30-40 mg triamcinolone acetonide (or its equivalent) per session[7,8]. Specific injection techniques such as steroid concentration, delivered volume, depth, and spacing of injections depend on both disease and patient characteristics and should be taken in consideration to achieve consistent results[8].

As a rough guide, 4 mg of triamcinolone is equivalent in anti-inflammatory activity to about 0.75 mg of betamethasone[7]. The dose is expressed in terms of the base, so it will be necessary to consider the equivalence between triamcinolone base and triamcinolone acetonide. In this case, 11 mg of triamcinolone acetonide is equivalent to 10 mg of triamcinolone base[7].

However, esterification generally alters potency, and compounds given at equivalent glucocorticoid doses may not have equivalent clinical effect[7].

In summary, thorough knowledge of available ILCS and appropriate conversion between alternative corticosteroids is essential for an effective and safe dermatological practice.

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