

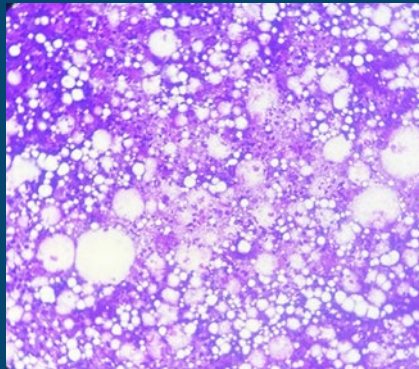
# PORTUGUESE JOURNAL OF DERMATOLOGY AND VENEREOLOGY

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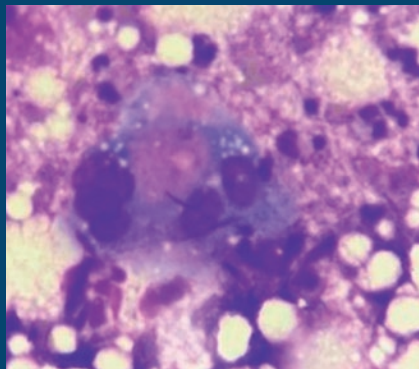
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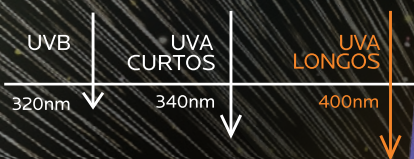
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1. Draelos ZD et al. Eficácia clínica de um novo hidratante com ceramidas para pele com xerose extrema e com prurido.  
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# Cutaneous manifestations of COVID-19 and vaccines for its prevention: a review of the existing literature

## *Manifestações cutâneas da doença COVID-19 e vacinas para a sua prevenção: uma revisão da literatura*

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### Abstract

The coronavirus SARS-CoV-2 first appeared in December 2019 in Wuhan, China, spreading rapidly as a novel pathogen primarily affecting the respiratory system. It soon evolved into a global pandemic that challenged healthcare systems worldwide. Intense research interest emerged early, revealing numerous cutaneous manifestations associated with both the virus itself – through its tropism for the angiotensin-converting enzyme 2 receptor – and the systemic complications it induced, such as cytokine storm and severe inflammatory reactions. Cutaneous findings were attributed to multiple mechanisms, including direct viral effects, immune dysregulation, drug reactions from early therapeutic regimens, and reactivation of autoimmune processes. Moreover, the vaccines developed to curb viral transmission and morbidity also presented certain dermatologic adverse effects, some resembling infection-induced manifestations, while others were linked to vaccine components and immune responses. This review summarizes the wide spectrum of skin manifestations associated with COVID-19 infection, vaccination, and the use of personal protective equipment, as well as the exacerbation of pre-existing dermatoses during the pandemic. Psychological stress and social isolation are also discussed as contributing factors to dermatologic morbidity. By synthesizing present scientific literature, this study provides a concise yet comprehensive overview of COVID-19- and vaccine-related skin manifestations, highlighting their clinical relevance and the need for further research on underlying mechanisms and management strategies.

**Keywords:** COVID-19. Skin. Vaccination. Adverse events.

### Resumo

O coronavírus SARS-CoV-2 surgiu pela primeira vez em dezembro de 2019 em Wuhan, na China, espalhando-se rapidamente como um novo agente patogênico que afeta principalmente o sistema respiratório. Logo evoluiu para uma pandemia global que desafiou os sistemas de saúde em todo o mundo. Um intenso interesse em pesquisa surgiu precocemente, revelando inúmeras manifestações cutâneas associadas tanto ao próprio vírus – através do seu tropismo pelo receptor da enzima conversora de angiotensina II (ACE2) – quanto às complicações sistêmicas que induziu, como a tempestade de citocinas e reações inflamatórias graves. Os achados cutâneos foram atribuídos a múltiplos mecanismos, incluindo efeitos virais diretos, desregulação imune, reações medicamentosas de regimes terapêuticos precoces e reativação de processos autoimunes.

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Além disso, as vacinas desenvolvidas para conter a transmissão viral e a morbidade também apresentaram certos efeitos adversos dermatológicos, alguns semelhantes às manifestações induzidas pela infecção, enquanto outros foram associados a componentes da vacina e respostas imunes. Esta revisão resume o amplo espectro de manifestações cutâneas associadas à infecção por COVID-19, à vacinação e ao uso de equipamentos de proteção individual, bem como à exacerbação de dermatoses pré-existentes durante a pandemia. O stress psicológico e o isolamento social também são discutidos como fatores contribuintes para a morbidade dermatológica. Ao sintetizar a literatura científica atual, este estudo fornece uma visão geral concisa, mas abrangente, das manifestações cutâneas relacionadas à COVID-19 e às vacinas, destacando sua relevância clínica e a necessidade de mais pesquisas sobre os mecanismos subjacentes e as estratégias de gestão.

**Palavras-chave:** COVID-19 e a pele. Vacinação contra a COVID-19. Manifestações cutâneas da COVID-19.

## Introduction

In December 2019, a new pathogen, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), began to spread, causing acute respiratory distress syndrome, initially in the Wuhan region of China. The coronavirus has had a significant impact on global health, with over 700 million cases worldwide according to the World Health Organization study. It is thought to originate from bats and is transmitted by droplets. Once the virus enters the body, its envelope protein S binds to the angiotensin 2 receptor on host cells and enters the cell by endocytosis. After entering the body, the virus multiplies, resulting in the secretion of cytokines, such as interleukin (IL)-8, IL-10, IL-12, tumor necrosis factor- $\alpha$ , Interferon- $\beta$ , leading to a pro inflammatory state.<sup>1</sup>

The angiotensin-converting enzyme 2 (ACE2) receptor is found in many cells in the human body, mainly in alveolar cells in the lungs, in the myocardium, in esophageal epithelial cells, in neurons, but also in the oral cavity, including epidermal cells and adnexal keratinocytes, and in vascular epithelial cells. This can explain the great variety and number of skin manifestations associated with coronavirus.<sup>2</sup> Another possible mechanism for the occurrence of skin manifestations is the hypersensitivity of the immune system induced by the coronavirus, which leads to the so-called cytokine storm, but also to the fact that the coronavirus creates a prothrombotic state in the body, which results in the formation of microthrombi and, by extension, the appearance of vasculitis.<sup>3</sup>

The frequency of these manifestations was different in various populations worldwide, with a smaller number of skin manifestations observed in Asia and Japan compared to Europe. Skin manifestations, initially described in Italy,<sup>4</sup> appeared in individuals of all ages and genders, with a slight predominance in women. Furthermore, some of them were associated with disease severity. However, it has been reported that skin manifestations may precede the onset of coronavirus

symptoms and be the first indication for the clinician or dermatologist that the patient has been infected with coronavirus. Accordingly, they may appear during the course of the disease or even after the symptoms have subsided, most commonly within a month of infection, and in some cases, cutaneous manifestations may be the only manifestation.<sup>5</sup>

To prevent further transmission of the coronavirus and stop the epidemic, RNA vaccines have been used. These vaccines have proven effective in limiting the epidemic and reducing hospitalizations, but they also have some dermatological adverse effects.<sup>6</sup> At the same time, the use of such extensive and skin-unfriendly protective equipment, as well as the reactivation of skin diseases that were reawakened by the immune response caused by the coronavirus, were issues that were unprecedented for the global community. Consequently, extensive interest was developed by researchers, as well as clinicians involved in the diagnosis and treatment of the coronavirus and its skin manifestations.<sup>7</sup> The methodology chosen in this paper is presented below.

## Methodology

For this study, a search of the relevant literature was conducted in PubMed/Medline and the search terms used were, "COVID-19 and the skin, dermatological manifestations of SARS-COVID, rashes and COVID-19 severity, influence of covid infection to the skin, COVID-19 and the nails and hair, skin diseases related with covid." At the same time, terms, such as skin complications of covid vaccines, adverse effects of the medicines for covid to the skin, skin disease related to covid protection in health workers and case reports, vasculitis and covid, erythema multiforme and covid, bullous diseases and covid and alopecia associated with coronavirus infection, as well as adverse effects of coronavirus vaccines were used without emphasizing any specific vaccine but an examination of all side effects was made.

During the literature search, a wide range of recent articles from 2021 onward that dealt with the topics under consideration emerged, and 91 of them were ultimately selected. The selection criterion was the completeness with which they addressed the topics under discussion, to facilitate the purpose of this work. In particular, the aim is to provide a concise but thorough presentation of the skin manifestations of coronavirus as a disease in itself, but also as an infection that can cause dermatological diseases even indirectly. Dermatological diseases may arise due to the use of the drugs that were and are used in the initial treatment of coronavirus, but also through immunological mechanisms and the action of cytokines observed in coronavirus, which can trigger autoimmunity and lead to an exacerbation of autoimmune skin diseases. According to the literature, such diseases include psoriasis and alopecia or bullous pemphigoid.<sup>8</sup>

In addition, healthcare professionals were involved in the chain of skin manifestations, as they used protective equipment to a large extent, the use of which was unprecedented for some countries that had not previously faced large epidemic waves. Finally, coronavirus vaccines were studied in terms of skin complications because they caused some complications that were particular and simulated the manifestations of the original disease, but in a smaller scope and severity. A total of 63 articles were thoroughly examined, which dealt with the issue of skin manifestations of coronavirus, even in various age groups, such as children and the elderly, who were more susceptible to skin manifestations. At the same time, reductions were made to the rest of the population, and various manifestations and mechanisms of these manifestations were analyzed to the extent that they have been understood to date by researchers. At the same time, 28 articles were examined that discussed the skin manifestations of coronavirus vaccines and how to deal with them. It is characteristic that during the study of the bibliography, the universality of the coronavirus phenomenon is extracted, giving impetus to researchers from all over the world to publish studies on the dermatological manifestations they observed in their clinics. Accordingly, at the national level, each country engaged in an effort to detect and track this pandemic, which was now an issue that concerned doctors of all specialties, including dermatologists.

## Discussion

Since the emergence of COVID-19 in late 2019, the infection has been associated with a broad range of cutaneous manifestations involving diverse morphological patterns and pathogenetic mechanisms. The dermatologic spectrum linked to SARS-CoV-2 encompasses rashes commonly seen in viral infections, immune-mediated conditions, vascular phenomena, and adverse effects arising from medications, vaccines, and pandemic-related interventions, such as personal protective equipment (PPE).<sup>1,9</sup>

A fundamental aspect of COVID-19 skin involvement relates to the viral tropism for ACE2 receptors, widely expressed in endothelial cells and keratinocytes. Viral entry and replication, coupled with dysregulated immune responses, including cytokine storm, microvascular injury, and complement activation, contribute to the cutaneous phenotypes observed during and after infection.<sup>10,11</sup> Furthermore, psychosocial stress, pharmacologic interventions, and widespread use of PPE during the pandemic have exacerbated pre-existing dermatoses and triggered new-onset conditions, highlighting the multifactorial nature of dermatologic sequelae.<sup>2</sup>

Among the earliest and most frequently reported skin manifestations is the morbilliform maculopapular rash, characterized by widespread erythematous macules and papules predominantly affecting the trunk and extremities, typically emerging within 2 weeks of symptom onset.<sup>1,9</sup> Although initially attributed to drug hypersensitivity from therapeutic agents, such as hydroxychloroquine or antivirals, subsequent observations in untreated patients confirmed a direct association with COVID-19 infection itself.<sup>6</sup> Histopathologic findings commonly reveal perivascular lymphocytic infiltrates and occasional microthrombi, supporting an immune-mediated rather than a purely cytopathic mechanism.<sup>12</sup>

Similarly, urticaria and, less frequently, angioedema constitute notable cutaneous reactions, often coinciding with systemic symptoms, such as fever or respiratory distress.<sup>13</sup> These lesions reflect mast cell activation and histamine release driven by immune dysregulation, cytokine release, or drug exposure.<sup>14</sup> Urticarial vasculitis, though rare, has also been documented, presenting with persistent wheals and histologic evidence of deposition of an immune complex, often containing viral particles and small-vessel inflammation.<sup>15</sup>

Pseudovaricella eruptions manifesting as monomorphic or diffuse vesicles have been described

predominantly in middle-aged adults with mild to moderate disease severity.<sup>1</sup> These lesions, frequently pruritic or hemorrhagic, appear either before or after respiratory symptoms and resolve spontaneously without scarring.<sup>9</sup> Histologic examination typically reveals keratinocyte necrosis, ballooning degeneration, and superficial perivascular infiltrates.<sup>16</sup>

Perhaps the most distinctive dermatologic signature of COVID-19 lies in its vascular manifestations, ranging from benign chilblain-like lesions (“COVID toes”) to severe ischemic complications.<sup>17</sup> Chilblain-like acral lesions, frequently affecting children and young adults with mild or asymptomatic disease, present as erythematous or violaceous plaques on the toes and fingers, occasionally accompanied by pain or pruritus.<sup>9</sup> While histologically indistinguishable from idiopathic pernio, their occurrence in warm climates and absence of cold exposure implicate interferon-mediated endothelial injury and microangiopathy.<sup>18</sup>

Conversely, acro-ischemia, livedo reticularis, retiform purpura, and even gangrene signify severe systemic involvement, correlating with coagulopathy, endothelial dysfunction, and complement activation seen in critical COVID-19 illness.<sup>19,20</sup> These lesions often portend a poor prognosis, especially in elderly patients with multisystem disease.<sup>1</sup>

Beyond exanthematous and vascular lesions, COVID-19 has triggered or exacerbated several immune-mediated dermatoses. Erythema multiforme, leukocytoclastic vasculitis, and pityriasis rosea-like eruptions have been repeatedly documented, reflecting post-viral immune dysregulation and molecular mimicry phenomena.<sup>12,21,22</sup> The reactivation of latent herpesviruses, particularly human herpesviruses-6/7 and varicella-zoster virus, further complicates the dermatologic landscape, resulting in increased incidence of herpes zoster and pityriasis rosea during the pandemic period.<sup>23</sup>

Similarly, multisystem inflammatory syndrome in children (MIS-C), a hyperinflammatory condition temporally associated with SARS-CoV-2 infection, frequently presents with mucocutaneous involvement, including polymorphous rashes, conjunctivitis, and periorbital edema.<sup>24</sup> Dermatologic signs in MIS-C not only aid early recognition but also parallel systemic hypercytokinemia, coronary vasculitis, and gastrointestinal inflammation.<sup>25</sup>

COVID-19 has also affected skin appendages, with telogen effluvium emerging as a common sequela several weeks after the acute infection.<sup>7</sup> Proposed mechanisms include cytokine-driven apoptosis of hair matrix

keratinocytes, microthrombotic injury to follicular vasculature, and systemic stress responses.<sup>26</sup> More acute anagen effluvium and alopecia areata flares have similarly been attributed to immune dysregulation and psychological stressors imposed by the pandemic.<sup>27</sup> Trichodynia, characterized by scalp dysesthesia with pain, pruritus, or burning sensation, frequently accompanies post-COVID-19 hair loss.<sup>9</sup>

Nail changes, such as Beau’s lines, transverse leukonychia, the “red half-moon” nail sign, and longitudinal melanonychia, have been increasingly recognized post-infection.<sup>28</sup> These findings, although non-specific, reflect transient growth arrest, vascular compromise, or drug exposure during illness.<sup>29</sup>

Mass vaccination campaigns worldwide have revealed diverse cutaneous reactions ranging from mild local responses to rare immune-mediated phenomena.<sup>3</sup> Immediate injection-site reactions, including erythema, swelling, and pain, represent the majority of events, typically resolving within days without sequelae.<sup>30</sup> Delayed large local reactions, colloquially termed “COVID arm,” present as pruritic erythematous plaques appearing a week post-vaccination, particularly with mRNA types.<sup>31</sup>

Urticaria, angioedema, and morbilliform eruptions have also been observed after both mRNA and viral vector vaccines, generally within days of administration.<sup>5</sup> Although most cases remain self-limited, rare instances of anaphylaxis needed vigilance, especially in individuals with prior allergy histories.<sup>3</sup> Reactivation of herpes zoster following vaccination, reported predominantly in elderly or immunocompromised recipients, is hypothesized to result from transient immune perturbations rather than direct viral effects.<sup>32</sup>

Autoimmune blistering diseases, including bullous pemphigoid and pemphigus vulgaris, have been described post-vaccination, primarily in older adults after mRNA vaccines.<sup>33</sup> Similarly, new-onset or flares of psoriasis, lupus erythematosus, and lichen planus underscore the capacity of vaccine-induced immune stimulation to unmask or exacerbate latent autoimmunity.<sup>34</sup> Nonetheless, the overwhelming consensus affirms that cutaneous adverse events remain infrequent, predominantly mild, and vastly outweighed by the benefits of vaccination in preventing severe COVID-19 outcomes.<sup>12</sup>

The prolonged use of PPE among healthcare workers and the general population has precipitated a surge in irritant and allergic contact dermatitis, acne mechanica (“maskne”), rosacea flares, and occupational hand eczema.<sup>2</sup> Occlusion, friction, sweating, and exposure

to disinfectants collectively disrupt the epidermal barrier, alter skin microbiota, and induce inflammatory dermatoses, emphasizing the occupational dermatology dimension of pandemic response.<sup>35</sup>

The cutaneous manifestations of COVID-19 and its vaccines reflect complex interactions between direct viral cytopathologic effect, immune dysregulation, vascular injury, pharmacologic triggers, and environmental factors. While most lesions remain self-limited with a favorable prognosis, certain phenotypes – including retiform purpura, acral ischemia, and multi-system inflammatory presentations – carry diagnostic and prognostic significance, warranting prompt recognition.<sup>1</sup>

For dermatologists, familiarity with this evolving spectrum aids differential diagnosis, guides biopsy and laboratory evaluation when indicated, and informs patient counseling regarding vaccine safety and expected reactions.<sup>9</sup> Moreover, understanding the temporal patterns, morphologic variants, and systemic associations of COVID-19-related skin findings enrich interdisciplinary collaboration across infectious disease, dermatology, pneumonology, rheumatology, pediatrics, and critical care settings.<sup>17</sup>

Finally, ongoing research into pathogenetic mechanisms underlying these manifestations promises to elucidate links between viral infections, immune activation, autoimmunity, and skin biology, offering broader insights into dermatologic science beyond the present pandemic context.<sup>12</sup>

## Conclusion

The COVID-19 pandemic has been one of the greatest challenges for healthcare systems worldwide, with the interest of the scientific community extending beyond the respiratory system to the dermatological findings of the disease.

As knowledge about the dermatological manifestations of COVID-19 is constantly enriched, it is becoming apparent that they may also function as diagnostic indicators, warning of the severity of the disease or even preceding respiratory symptomatology.

COVID-19 vaccines, although effective, are not without dermatological side effects. Particular attention is required in patients with pre-existing skin or autoimmune diseases.

The need for further research is obvious and multifaceted. Initially, it is necessary to establish national and international registries to classify and document skin manifestations associated with COVID-19 and

vaccines. Across the collection of big data, a clearer epidemiological profile can be formed, which will help both in prevention and treatment.

In addition, long-term patient follow-up studies are needed to determine whether certain skin diseases develop into a chronic form or reappear after new exposure to the virus or booster vaccinations. The association of the cutaneous immune response with the type of vaccine (mRNA, vector-based, etc.) is also an area of significant research interest.

Particular emphasis should be placed on the education of health professionals – and especially general practitioners and dermatologists – for the early recognition of cutaneous signs, which often precede the full manifestation of the infection or are the only manifestations in asymptomatic patients.

Furthermore, the development of new, more targeted and safer vaccines with minimal dermatological impact, as well as the investigation of prophylactic and therapeutic dermatological interventions to address complications, should be priorities for the coming period.

Finally, strengthening interdisciplinary collaboration between dermatologists, infectious disease specialists, immunologists, and epidemiologists can offer substantial solutions and strengthen the comprehensive approach to addressing COVID-19 and its multifaceted impacts.

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## Conflicts of interest

None.

## Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.


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# Genital psoriasis: clinical, epidemiological and therapeutic aspects

## *Psoríase genital: aspectos clínicos, epidemiológicos e terapêuticos*

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### Abstract

Genital psoriasis presents as erythematous plaques with variable scaling and symptoms such as pruritus, burning, and dyspareunia, which can significantly affect the quality of life, psychological well-being, and sexual health of affected patients. It is estimated that approximately 1.2-2.5% of the population has psoriasis; however, genital involvement is not widely described and may be underestimated, as these areas are often not actively questioned or assessed during the clinical examination. This article aims to explore the clinical aspects of genital psoriasis, including its prevalence, impact on sexual health, and treatment options.

**Keywords:** Genital diseases. Genital psoriasis. Psoriasis. Therapy.

### Resumo

A psoríase genital manifesta-se como placas eritematosas com descamação variável e sintomas como prurido, ardor e dispareunia, que podem afetar significativamente a qualidade de vida, o bem-estar psicológico e a saúde sexual dos pacientes acometidos. Estima-se que aproximadamente 1.2% a 2.5% da população apresente psoríase; contudo, o acometimento genital não é amplamente descrito e pode ser subestimado, uma vez que essas áreas frequentemente não são ativamente investigadas ou avaliadas durante o exame clínico. Este artigo tem como objetivo explorar os aspectos clínicos da psoríase genital, incluindo sua prevalência, impacto na saúde sexual e opções terapêuticas.

**Palavras-chave:** Doenças genitais. Psoríase genital. Psoríase. Terapêutica.

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## Introduction

Psoriasis is a chronic, immune-mediated inflammatory disease characterized by erythematous, scaly, infiltrated, and pruritic plaques on the skin. It typically affects the extensor surfaces, scalp, palms, soles, and nails; however, it can involve any area of the integument. It has a negative impact on the quality of life of affected patients and can be associated with comorbidities such as psoriatic arthritis.<sup>1</sup>

Genital psoriasis usually presents as erythematous, well-defined plaques with varying degrees of desquamation. Symptoms such as pruritus, burning, and dyspareunia have been reported.<sup>2</sup> Therefore, genital psoriasis can significantly affect the quality of life, psychological well-being, and sexual health of affected patients.<sup>3</sup>

In Brazil, the estimated prevalence of psoriasis ranges from 1.2% to 2.5%.<sup>4,5</sup> However, genital involvement is not widely described. It is estimated that genital involvement occurs in more than two-thirds of patients;<sup>6</sup> however, this proportion may be underestimated, as these areas may not be actively questioned or assessed during the clinical examination.<sup>7</sup>

This paper aims to explore clinical aspects of genital psoriasis, including its prevalence, impact on sexual health and treatment options.

## Epidemiology

Among the various dermatoses that can affect the genitals, psoriasis is the most common.<sup>8</sup> A systematic review conducted by Meeuwis et al., including 18 studies and a total of 22,116 patients with psoriasis, showed that approximately 63% of patients will present some genital involvement during the course of the disease. This proportion increases to 79% when the patient has the flexural or inverted clinical form of the disease.<sup>6</sup>

In a prospective study totaling 776 patients with psoriasis, 43.2% of the patients had genital involvement.<sup>2</sup> An Indian study examining 852 patients with psoriasis reported a lower prevalence of 11.7%.<sup>9</sup> A prospective observational study with a total of 262 patients, 42% Chinese, 36.6% Malay and 21.4% Indian or other nationalities, showed 46.1% genital involvement by psoriasis currently or previously to the study.<sup>7</sup> Curiously, this study also identified that being Chinese was a risk factor for genital psoriasis when compared to the other ethnicities included.<sup>7</sup>

Men are more frequently affected by genital psoriasis than women<sup>6,7,10</sup> and it manifests simultaneously with

lesions on other parts of the body in the majority of cases, with isolated genital involvement being reported in only 2-5% of cases.<sup>11</sup> More severe cases, as assessed by the psoriasis area and severity index (PASI), and the greater use of systemic therapies have been associated with genital psoriasis.<sup>2</sup> A Swiss study evaluated 109 children with psoriasis, and genital involvement was present in around 40% of them and was often the first manifestation of the disease.<sup>12</sup> Circumcision apparently does not influence the development of genital psoriasis in men.<sup>2</sup>

## Clinical manifestations

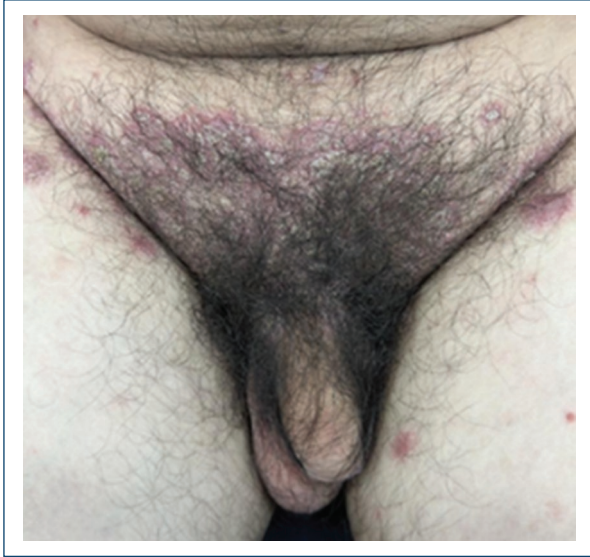
The most characteristic lesions are well-defined erythematous plaques with minimal infiltration. Unlike lesions in other regions of the body, desquamation may be absent, possibly due to increased local humidity and friction.<sup>13</sup> However, typical scales may be present in more keratinized areas (Fig. 1).<sup>14</sup> The areas mostly affected in men include the body of the penis, the scrotum, and, less commonly, the glans (Fig. 2). In women, the labia majora are the most commonly affected areas and are often symmetrically involved, followed by the perineum.<sup>2</sup>

Pruritus is the main symptom of genital psoriasis, reported by more than 86% of patients; however, around half of the cases experience pain, burning, and discomfort during sexual intercourse due to the presence of fissures.<sup>2</sup> Due to the Koebner phenomenon, genital psoriasis can be aggravated by irritation caused by urine and feces, tight clothing, and trauma from sexual intercourse.<sup>15</sup>

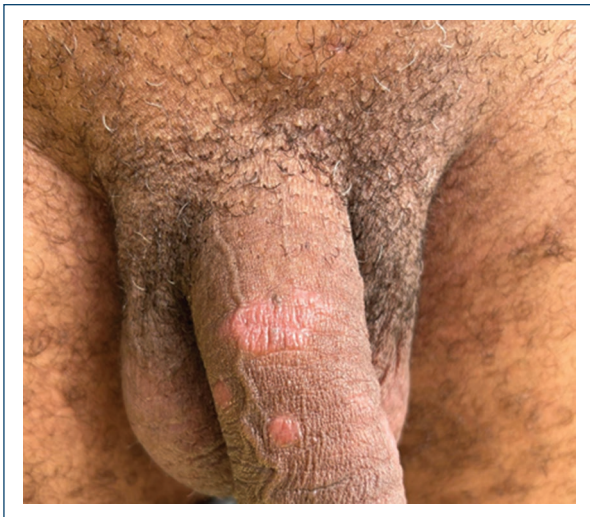
Genital psoriasis is not a static disease; in general, its worsening occurs in parallel with the progression of non-genital lesions, although there are exceptions.<sup>16</sup> The main worsening factors traditionally described include emotional stress, trauma, some medications, and friction (related to sexual activity or wearing tight clothing).<sup>3</sup> Studies show that up to 34% of patients experience post-coital worsening.<sup>2,17</sup>

The diagnosis of genital psoriasis is essentially clinical, and biopsy is avoided in these cases due to the sensitivity of the area. Therefore, as a non-invasive method, dermoscopy may serve as an additional diagnostic tool. Dotted vessels and dilated, tortuous capillaries distributed over a homogeneous reddish background represent the most frequently described pattern.<sup>18</sup>

Psoriasis is a condition that generally does not lead to tissue fibrosis; however, Albert et al. described two cases of female patients with long-term genital psoriasis who developed fibrosis and loss of the labia minora.<sup>19</sup>



**Figure 1.** Erythematous and scaly plaques affecting the base of the penis and the pubic region of a male patient with psoriasis.



**Figure 2.** Erythematous plaques affecting the dorsal region of the penile body in a male patient with psoriasis.

Secondary infection by bacteria, fungi, or viruses is relatively common and can aggravate symptoms or cause atypical manifestations. Therefore, in the event of clinical suspicion, the infection should be treated promptly.<sup>13</sup> A retrospective observational study showed that more than a third of patients with genital psoriasis had positive swabs for *Candida albicans* or *Staphylococcus* spp.<sup>20</sup>

## Differential diagnoses

The differential diagnosis of genital psoriasis encompasses a broad spectrum of inflammatory and infectious dermatoses, including candidiasis, contact dermatitis, lichen planus, lichen sclerosus, and sexually transmitted infections, all of which may exhibit overlapping clinical features in the genital region.<sup>11,21</sup> Genital psoriasis may pose a significant diagnostic challenge, particularly when lesions are isolated and not accompanied by extragenital manifestations.<sup>11,22</sup> In such circumstances, clinical overlap with premalignant and malignant conditions must be considered. Squamous cell carcinoma, including erythroplasia of Queyrat, may closely mimic genital or inverse psoriasis, potentially leading to diagnostic misinterpretation and delayed treatment.<sup>23</sup> Although the diagnosis of genital psoriasis is typically clinical, current evidence supports a low threshold for performing a skin biopsy in cases of solitary, persistent, atypical, or treatment-refractory genital lesions, to exclude malignancy and ensure diagnostic accuracy.<sup>11,22,23</sup>

## Severity assessment tools

The assessment tools traditionally used in psoriasis may not be suitable for the genital form of the disease. The PASI and body surface area are tools that depend on the area of the affected body surface, so in genital psoriasis alone, they will not be able to demonstrate the severity of the disease adequately.<sup>24</sup> Although the dermatology life quality index includes, in item 9, the impact of the disease on sexual life, it is not specific to genital psoriasis.<sup>25</sup> Therefore, more specific tools have been developed in order to refine this assessment, including the genital psoriasis sexual frequency questionnaire and the genital psoriasis symptoms scale.<sup>26</sup>

## Treatment

The treatment of genital psoriasis is challenging due to the particularities of the skin in this area. Patients should be informed that the disease is neither transmissible nor the result of poor hygiene. In addition, teaching them to use non-irritating cleansers, topical medication in sufficient quantities, and moisturizing the area helps with the therapeutic response. Furthermore, the use of intimate lubricants during sexual intercourse reduces friction and, consequently, the risk of Koebner's phenomenon.<sup>27</sup>

Therapy with topical corticosteroids, alone or in combination with systemic drugs, has been shown to be the initial treatment of choice for genital psoriasis.<sup>28</sup> As the skin is thinner and subject to natural occlusion, percutaneous absorption is increased;<sup>29</sup> therefore, the use of low-potency topical corticosteroids, such as hydrocortisone, is recommended, and their effectiveness has been demonstrated in prospective and retrospective studies.<sup>6,20,30,31</sup> It is recommended not to extrapolate the use time of four continuous weeks to minimize the risk of well-known adverse events, including skin atrophy, telangiectasias, and stretch marks.<sup>28</sup>

Although low or medium potency corticosteroids are preferable for sensitive areas such as the genitals, high potency corticosteroids may be indicated for short periods in moderate to severe cases or to induce an initial clinical response.<sup>20</sup> Formulations with Vitamin D analogues, such as calcipotriol, can be used in conjunction with corticosteroids or even after their use.<sup>31</sup>

Topical calcineurin inhibitors (TCI), such as tacrolimus and pimecrolimus, are alternatives for long-term topical therapies. They are associated with milder and more manageable adverse effects, as they do not interfere with collagen synthesis, so the risk of skin atrophy is significantly lower compared to corticosteroids.<sup>32</sup> However, they can cause pruritus and burning at the application site.

Although the indication for the treatment of psoriasis is not included in the package leaflet for TCIs, some studies have shown benefits. A study by Bissonnette et al. showed a satisfactory response and tolerability in a group of 12 men with genital psoriasis who used tacrolimus 0.1% ointment for 8 weeks.<sup>33</sup> A study of 10 patients with facial and genital psoriasis showed that tacrolimus 0.1% ointment improved the symptoms of genital psoriasis after 12 weeks of use.<sup>34</sup>

Topical Vitamin D analogs, such as calcitriol and calcipotriol, are another class of drugs that can be used for a long time in genital and inverted psoriasis. In general, studies show that both calcitriol and calcipotriol are safe, but less effective than corticosteroids or TCI.<sup>35</sup> A randomized direct comparison study between calcitriol 3 µg/g ointment and calcipotriol 50 µg/g ointment, both applied twice a day, showed that calcitriol was not only more effective, but also better tolerated in the treatment of inverted psoriasis.<sup>36</sup>

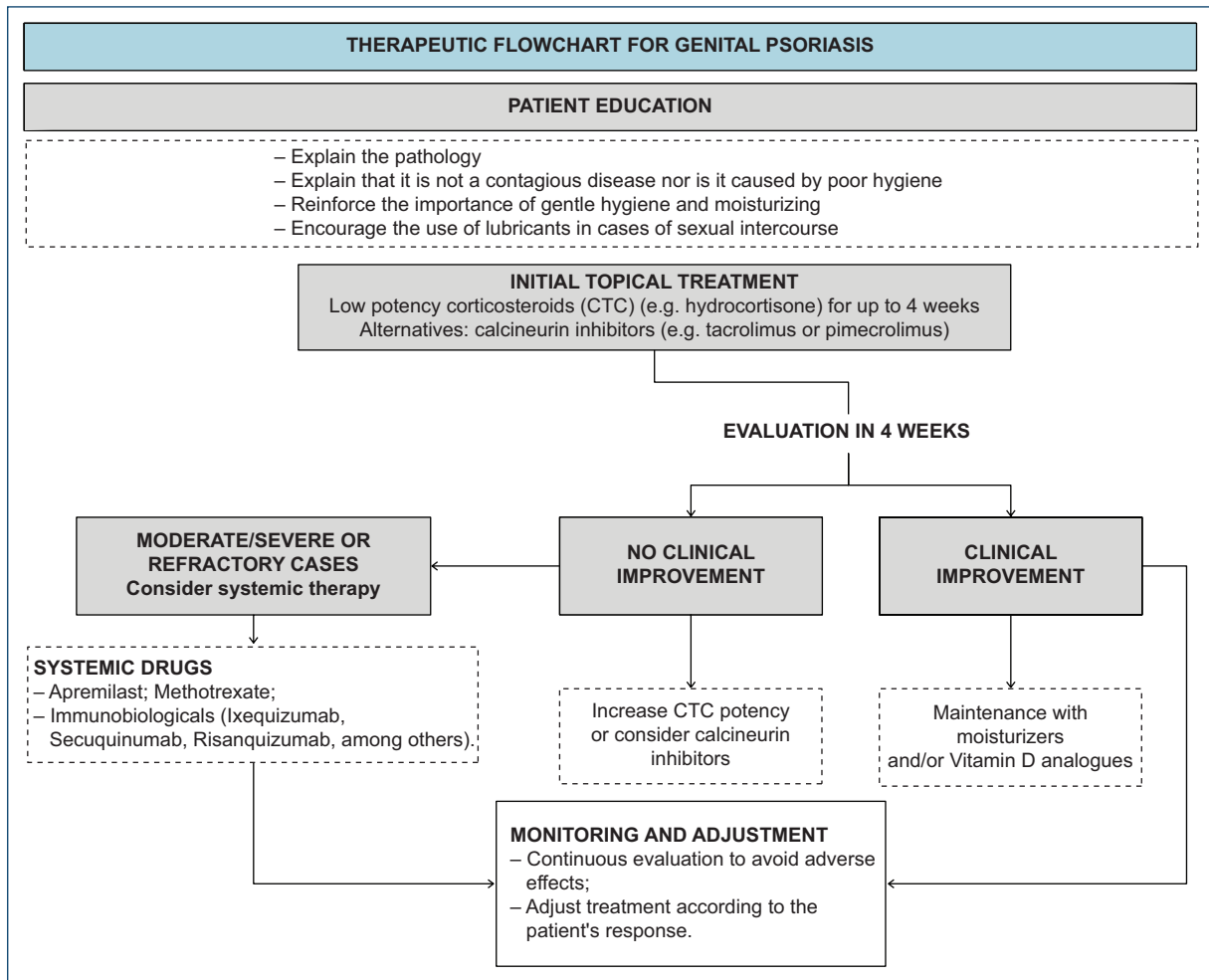
In general, phototherapy is not indicated for the treatment of genital psoriasis due to the increased risk of skin cancer in this area. A prospective study of 892 men with psoriasis exposed for a long time to psoralens and ultraviolet A (PUVA) radiation had an increased risk

of tumors in the penis and scrotum, particularly squamous cell carcinoma. Furthermore, even after controlling for levels of exposure to PUVA, high levels of exposure to ultraviolet B radiation were also associated with an increased risk of genital cancer.<sup>37</sup>

Up to now, there have been no large clinical trials evaluating the efficacy and safety of traditional oral systemic therapies for genital psoriasis. One study demonstrated successful treatment with methotrexate, but a second described only a partial response to the drug.<sup>12,20</sup> In addition, dapsone was used with a satisfactory response in two cases of pustular psoriasis affecting the skin of the penis.<sup>38,39</sup> On the other hand, a randomized, placebo-controlled study showed that apremilast, an oral phosphodiesterase-4 inhibitor, improved the quality of life of patients with psoriasis involving limited and spatial areas, including the genitals.<sup>40</sup> More specifically, another recent study evaluated the response to apremilast in patients with genital psoriasis, which also showed benefits.<sup>41</sup>

At present, the biologic agent with the specific indication for the treatment of genital psoriasis is ixekizumab, which is a high-affinity monoclonal antibody against interleukin (IL)-17A. Several studies have shown significant improvement in lesion appearance, pruritus, sexual health, and quality of life in patients with resistant genital psoriasis treated with ixekizumab.<sup>42-45</sup> In addition, a Phase III, randomized, placebo-controlled clinical study demonstrated long-term efficacy and safety up to week 52 of treatment with ixekizumab.<sup>44</sup> Patients received subcutaneous injections of 80 mg of ixekizumab (n = 74) or placebo (n = 74) every 2 weeks after an initial dose of 160 mg at week 0 until week 12; after which the study entered an open phase in which all patients received 80 mg every 4 weeks until week 52. As a result, in the initial phase of the study, 73% of the patients who received the drug achieved total or almost total improvement. Similarly, 79% of the patients who were initially in the placebo group achieved similar results at the end of week 52.

In addition to clinical trials, a real-life study involving 1978 patients with moderate to severe psoriasis, of whom around 25% had genital involvement, showed that in this subgroup of patients the IL-17A inhibitor biologics (ixekizumab and secukinumab) were significantly more effective than the other biologics agents used by the patients in the study (guselkumab, risankizumab, ustekinumab and adalimumab).<sup>46</sup> When compared individually with ixekizumab, ustekinumab, and guselkumab were the least effective of the biologics agents used.



**Figure 3.** Therapeutic flowchart for genital psoriasis.

Similarly, in a real-life study of 255 patients with psoriasis treated with adalimumab, etanercept, or ustekinumab, genital psoriasis was associated with complete resolution of the condition (PASI100) when patients were treated with adalimumab.<sup>47</sup> In this context, Orsini et al. showed satisfactory results in a real-life scenario in which patients with psoriasis were treated with risankizumab. Of a total of 202 patients, 72 had genital involvement. At the end of weeks 16, 28, and 52 of risankizumab use, 85%, 93% and 100% showed total or almost total improvement, respectively.<sup>48</sup>

Finally, the Italian GULLIVER study, a 12-week interim analysis, evaluated the efficacy and safety of guselkumab, a fully human monoclonal antibody targeting the p19 subunit of IL-23, in the treatment of genital and facial psoriasis. With 351 patients included, 204 of whom had genital psoriasis, it was observed that 76.5% of patients achieved an static physician's global assessment score of 0 (clean) or 1 (almost clean) in the genital

area after 12 weeks of treatment. As well as a significant improvement in erythema, thickness, and scaling scores in genital lesions, guselkumab also demonstrated a favorable safety profile, with only two mild and transient treatment-related adverse events. These results suggest that the IL-23 inhibitor is an effective and safe therapeutic option for patients with genital psoriasis.<sup>49,50</sup> The management of genital psoriasis can be summarized in figure 3.

## Conclusion

Genital psoriasis is a chronic and recurrent inflammatory disease, with a possibly underestimated prevalence, which significantly impacts patients' physical, emotional, and sexual health. Its treatment involves considerable challenges; however, traditional therapies such as low-potency corticosteroids may be used as an initial approach. In addition, calcineurin inhibitors

and Vitamin D analogues are alternatives for long-term topical therapies, due to their safety profile. More recent studies involving biologic therapies, particularly IL-17A and IL-23 inhibitors, have shown promising results in the management of refractory genital psoriasis, demonstrating improvements in both clinical outcomes and quality of life.

## Funding

None.

## Conflicts of interest

None.

## Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable 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 or creation of the content of this manuscript.

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# Evaluation of dyslipidemia among patients with chronic spontaneous urticaria: a cross-sectional study

## Avaliação da dislipidemia em pacientes com urticária crônica espontânea: um estudo transversal

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### Abstract

**Objective:** The objectives of this study were to compare the lipid profiles of patients with chronic spontaneous urticaria (CSU) and healthy controls, to identify which lipid parameter is most altered in CSU, and to determine the age and sex group among CSU patients most commonly affected by dyslipidemia. **Methods:** This cross-sectional study included 30 CSU cases and 30 age-and sex-matched controls. Serum lipids were analyzed through an autoanalyzer; groups were compared using the t-test and  $X^2$  test. **Results:** In our study, dyslipidemia appeared in 53.3% of cases of CSU versus 36.6% of controls. Triglycerides (TG) were significantly elevated in cases compared to controls ( $p = -0.036$ ), and very low density lipoprotein (VLDL) levels were higher in cases than controls ( $p = -0.004$ ). The mean age of participants with dyslipidemia was  $31.56 \pm 7.57$  years, with the majority belonging to the 26-35-year age group. **Conclusion:** This study demonstrates a notable risk of developing dyslipidemia in CSU patients, with TG and VLDL being the most affected parameters.

**Keywords:** Chronic spontaneous urticaria. Chronic inflammation. Auto-immune. Pro-inflammatory cytokines. Dyslipidemia.

### Resumo

**Objetivo:** Os objetivos deste estudo são comparar os perfis lipídicos dos doentes com urticária crônica espontânea (UCE) e dos controlos saudáveis, identificar qual o componente lipídico mais alterado na UCE e determinar a faixa etária e o sexo entre os doentes com UCE mais comumente afetados pela dislipidemia. **Métodos:** Este estudo transversal incluiu 30 casos de UCE e 30 controlos emparelhados por idade e sexo. Os lípidos séricos foram analisados através de um autoanalisador; os grupos foram comparados através dos testes t e qui-quadrado. **Resultados:** No nosso estudo, a média de idades dos casos com dislipidemia foi de  $31,56 \pm 7,57$  anos, com a maioria na faixa etária dos 26 aos 35 anos, e a dislipidemia apareceu em 53,3% dos casos versus 36,6% dos controlos. Os triglicéridos apresentaram-se significativamente elevados nos casos em comparação com os controlos ( $p = 0.036$ ), e os níveis de VLDL foram mais elevados nos casos do que nos controlos ( $p = 0.004$ ). **Conclusão:** Este estudo demonstra um risco considerável de desenvolvimento de dislipidemia em doentes com UCE, sendo os triglicéridos e o VLDL os mais afetados.

**Palavras-chave:** Urticária crônica espontânea. Inflamação crônica. Autoimune. Citocinas pró-inflamatórias. Dislipidemia.

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## Introduction

Chronic urticaria is a distressing condition commonly encountered by dermatologists globally, characterized by recurrent transient itchy wheals and/or angioedema lasting for more than 6 weeks. It can be further categorized into spontaneous or inducible.

The prevalence of chronic spontaneous urticaria (CSU) is estimated to be around 0.5-1% of the general population.<sup>1</sup> CSU typically peaks around the fourth decade of life and is more common in females than in males.

CSU occurs due to the interplay of various causative factors that act synergistically or sequentially, either by independent or interlinked mechanisms. This results in mast cell activation and release of preformed vasoactive mediators and newly synthesized pro-inflammatory molecules.<sup>2</sup>

Even though the pathomechanism of CSU is multifarious, autoimmunity plays a significant role, further justified by the association of CSU with other auto-immune conditions such as auto-immune thyroid disease,<sup>3</sup> vitiligo, pernicious anemia, and rheumatoid arthritis.<sup>4</sup> The most accepted pathogenic mechanism of CSU is the presence of autoantibodies on a background of chronic inflammation. Immunoglobulin E (IgE) antibodies against auto-antigens, namely interleukin (IL)-24 or thyroperoxidase (type 1 autoallergic CSU), are detected in several patients, and immunoglobulin G autoantibodies against IgE and FcεRI (type 2 auto-immune CSU) are detected in about 30-50% of the patients.<sup>5</sup> The binding of auto-antibodies to mast cells results in complement activation, and the generation of C5a anaphylatoxin facilitates or augments mast cell degranulation.<sup>6</sup> This leads to the release of histamine, proteases, cytokines, and other metabolites of arachidonic acid, thus leading to chronic inflammation.

Moreover, abnormal innate immunity, dysregulated intracellular signaling pathways in basophils and mast cells, and concurrent activation of the inflammatory response and coagulation system also contribute to the development of CSU.<sup>2,7,8</sup>

CSU is known to be associated with low-grade chronic inflammation, as depicted by mast cell degranulation in the skin, infiltration of T cells, eosinophils, and neutrophils, as well as elevated levels of pro-inflammatory cytokines in circulation.<sup>9</sup> Inflammation plays a crucial role in connecting the immune system with hypercholesterolemia, which is a contributing factor to the elevated risk of cardiovascular disease.<sup>10</sup> The levels of pro-inflammatory cytokines reflect the severity of lipid

abnormalities.<sup>8</sup> Symptoms of auto-immune diseases were found to be improved by cholesterol-lowering treatments such as a low-fat diet or statins.<sup>11</sup>

Moreover, increased body mass index (BMI), or obesity, frequently found in CSU patients, can further lead to changes in lipid metabolism. Adipose tissue acts as an active endocrine organ, releasing pro-inflammatory cytokines that may exacerbate the skin condition and alter the lipid profile. Mast cells have been found to cause endothelial inflammation and alter the lipid profile, thereby promoting the development of atherosclerosis.<sup>12-15</sup>

As chronic inflammatory skin diseases are recognized as risk factors for dysmetabolic syndrome, it is plausible that CSU also plays a role in the development of dyslipidemia.<sup>16,17</sup> Elevated levels of pro-inflammatory cytokines such as tumor necrosis factor- $\alpha$  and IL-6<sup>18</sup> can cause dyslipidemia by reducing the breakdown and removal of cholesterol<sup>19</sup> and by inhibiting the activity of adipocyte lipoprotein lipase,<sup>20</sup> respectively.

Cytokines play a role in elevating fatty acid synthesis and reducing their oxidation within the liver. They also stimulate the breakdown of fats in adipose tissue, leading to increased triglyceride (TG) synthesis in the liver. Greater TG availability results in heightened production and release of very low-density lipoprotein (VLDL).<sup>21</sup>

Henceforth, CSU and dyslipidemia might be connected through an underlying inflammatory process or immune system dysregulation. A recent study conducted in Germany by Weller et al. revealed that metabolic disorders impacting lipoproteins were often cited as comorbidities in individuals with chronic urticaria,<sup>22</sup> and a study by Viswanath et al. showed TG to be significantly elevated in patients with CSU.<sup>23</sup> Furthermore, the composition and distribution of high-density lipoprotein (HDL) particles are reported to be significantly altered in CSU, affecting their ability to modulate immune cell responses.<sup>24</sup> Low-density lipoprotein (LDL) is more readily absorbed by smooth muscle cells and macrophages when it binds to the leftover granules of mast cells.<sup>14</sup>

However, fewer studies have evaluated the exact potential link between CSU and dyslipidemia. Hence, after thoroughly going through the conflicting literature on dyslipidemia and CSU, we devised a plan to assess serum lipid levels in CSU patients and determine whether the association exists in our demographics.

The objectives of this study are to compare the lipid profiles of patients with CSU and healthy controls, to identify which lipid parameter is most altered in CSU,

and to determine the age and sex group among CSU patients most commonly affected by dyslipidemia.

## Methods

This cross-sectional study included 30 cases of CSU and 30 age- and sex-matched healthy controls seen at the dermatology outpatient department of a tertiary care hospital.

Individuals aged 15-45 years who provided informed consent were included, with cases comprising those with a clinical diagnosis of CSU and controls free of skin or systemic diseases. Exclusion criteria included patients with dyslipidemia, conditions predisposing to dyslipidemia (such as diabetes, hypothyroidism, chronic kidney or liver disease, and other endocrine disorders), those on lipid-lowering medications (such as statins or fibrates), and individuals taking drugs that could alter serum lipid levels (such as diuretics, retinoids, anabolic steroids, glucocorticoids, estrogens, cyclosporine,  $\beta$ -blockers, and antipsychotics). In addition, patients with chronic skin or rheumatological diseases, a family history of dyslipidemia or myocardial infarction, and pregnant or breastfeeding women were excluded.

Consent was obtained from the subjects after explaining the purpose of the research. Under sterile conditions, blood samples were collected in a tube without an anticoagulant after 10 h of fasting and then sent for analysis.

Serum lipid profile was conducted by an autoanalyzer and included total cholesterol (TC), TG, HDL-C, LDL-C, VLDL, and cholesterol/HDL ratio (TC/HDL). Normal reference values are as follows: < 200 mg/dL for TC, < 150 mg/dL for TG, > 40 mg/dL for HDL, < 130 mg/dL for LDL, < 30 mg/dL for VLDL, and < 3.5 for the TC/HDL ratio.

Data obtained were tabulated and assessed by IBM Statistical Package for Social Sciences V20 software. Continuous variables were outlined using frequency, mean, and standard deviation. Means among groups were compared using an independent t-test, and proportions were compared using the  $X^2$  test. A  $p < 0.05$  was considered statistically significant.

This study was reviewed and approved by the institutional ethics committee of the tertiary care hospital where the research was conducted (IEC No: IEC/KMCH/2023/71).

## Results

Our study included 30 CSU cases (12 males and 18 females) and 30 age- and sex-matched controls

(15 males and 15 females) between 15 and 45 years of age. The overall mean age of cases was  $29.4 \pm 8.1$  years, whereas that of controls was  $30.3 \pm 8.6$  years.

Dyslipidemia was detected in 53.3% of CSU cases and 36.6% of controls ( $p = 0.299$ ), with CSU cases having the highest number of individuals with alterations and higher mean values within the TG and VLDL.

We observed elevated TG in 50% (15 patients) of CSU cases compared to 26.6% (8 patients) of controls in our study (Table 1). Mean levels of TG were remarkably higher in CSU cases ( $161.1 \pm 74.3$ ) than in controls ( $128.9 \pm 34.3$ ), with  $p = 0.036$  (Table 2). VLDL was elevated in 12 patients (40%) with CSU, compared to 7 (23.3%) in controls. Statistically significantly higher values of VLDL were noted in CSU cases ( $33.7 \pm 20.6$ ) compared to controls ( $21.5 \pm 8.93$ ), with  $p = 0.004$  (Table 2). A high cholesterol/HDL ratio was observed in 16 CSU patients (53.3%) and in 11 controls (36.6%), but the mean value of this ratio was not significantly different ( $3.83 \pm 0.803$  vs.  $3.75 \pm 0.82$ ). No significant differences were observed in the number of patients with changes in TC, LDL, or HDL between patients and controls. Furthermore, the mean levels of TC, HDL, LDL, and TC/HDL between patients and controls did not differ statistically significantly in our investigation (Tables 1 and 2).

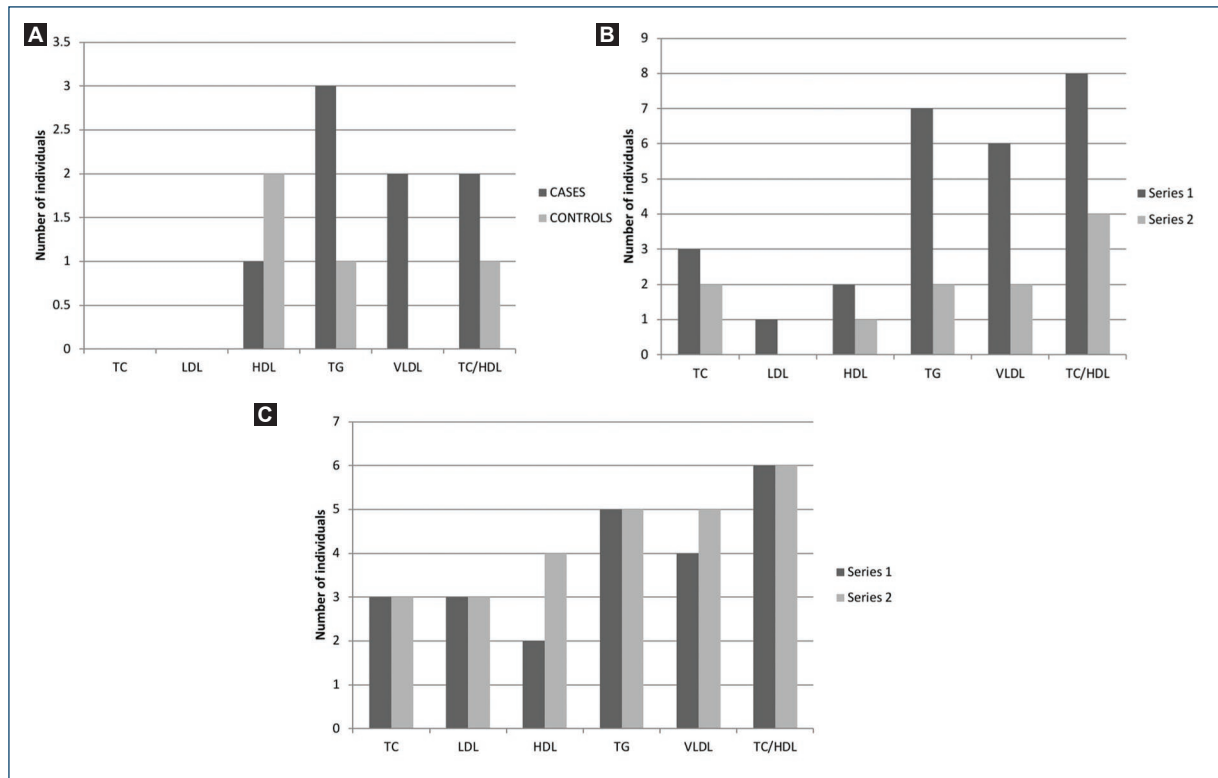
In the CSU group, dyslipidemia affected 9 males (30%) and 7 females (23.3%), whereas in the control group, it affected 6 males (20%) and 5 females (16.7%) (Table 3).

The mean age of CSU cases with dyslipidemia was  $31.56 \pm 7.57$  years compared with  $32.36 \pm 8.41$  in controls. Most cases of dyslipidemia in the CSU group with elevated TG and VLDL occurred in the 26-35 year age group (26.6%), followed by 36-45 (16.7%) and 15-25 years (10%), whereas the 36-45 year age group (16.7%) was the most affected in controls (Table 3 and Fig. 1).

## Discussion

Our sample of CSU, with the age of disease distribution between 15 and 45 years, a mean age of around 30, and a significant female predominance (18 patients), is in accordance with the previous studies on the demographics of CSU.<sup>25,26</sup>

Similar to the observations of Ye et al.,<sup>27</sup> our study found a slight predominance of dyslipidemia in males compared to females among cases. The mean age of distribution among cases with dyslipidemia was  $31.56 \pm 7.57$  years. Dyslipidemia showed the highest



**Figure 1.** Altered lipid profile in different age groups. **A:** 15-25 year age group. **B:** 26-35 year age group. **C:** 36-45 year age group.

**Table 1.** Number of cases and controls with altered serum lipids and lipoproteins

Lipid parameter	CSU (%)	Controls (%)	p
Cholesterol	6 (20)	5 (16.6)	1.000
LDL	4 (13.3)	3 (10)	1.000
HDL	5 (16.6)	7 (23.3)	0.748
TC/HDL	16 (53.3)	11 (36.6)	0.299
Triglycerides	15 (50)	8 (26.6)	0.110
VLDL	12 (40)	7 (23.3)	0.267

TC: total cholesterol; LDL: low density lipoprotein; HDL: high density lipoprotein; TG: triglycerides; TC/HDL: total cholesterol/high density lipoprotein; VLDL: very low density lipoprotein; CSU: chronic spontaneous urticaria.

**Table 2.** Mean values of lipid profile among cases and controls

Lipid profile	CSU cases (mean $\pm$ SD)	Controls (mean $\pm$ SD)	p
Cholesterol	177.4 $\pm$ 31.4	170.2 $\pm$ 31.4	0.379
LDL	97.9 $\pm$ 24.5	99.3 $\pm$ 23.9	0.824
HDL	47.33 $\pm$ 8.84	46.10 $\pm$ 7.60	0.569
TC/HDL	3.83 $\pm$ 0.80	3.75 $\pm$ 0.82	0.702
Triglycerides	161.1 $\pm$ 74.3	128.9 $\pm$ 34.3	0.036
VLDL	33.7 $\pm$ 20.6	21.5 $\pm$ 8.93	0.004

TC: total cholesterol; LDL: low density lipoprotein; HDL: high density lipoprotein; TG: triglycerides; TC/HDL: total cholesterol/high density lipoprotein; VLDL: very low density lipoprotein; SD: standard deviation; CSU: chronic spontaneous urticaria.

incidence in the 26-35 year age group, with the 36-45 and 15-25 year age groups following suit.

Dyslipidemia was present in 53.3% of cases, and the elevation in the mean serum TG was found to be statistically significant in cases ( $p = 0.036$ ) when compared to controls. This observation is consistent with the study conducted by Vishwanath et al.<sup>23</sup>

There is a statistically significant elevation in the mean serum VLDL levels in cases compared to controls. However, the changes in TC, HDL, LDL, and TC/HDL were not statistically significant in cases compared to controls. These findings were in accordance with the observations of Vishwanath et al.,<sup>23</sup> but are discordant with the results of studies done by Amin

**Table 3.** Sociodemographic profile among CSU cases and controls with dyslipidemia

Sociodemographic profile	CSU cases with dyslipidemia (%)	Controls with dyslipidemia (%)	p
Male	9 (30)	6 (20)	0.552
Female	7 (23.3)	5 (16.7)	0.748
Total	16 (53.3)	11 (36.7)	0.299
Age groups			
15-25 years	3 (10)	2 (6.7)	1.000
26-35 years	8 (26.6)	4 (13.3)	0.333
36-45 years	5 (16.7)	5 (16.7)	1.000
Age (mean $\pm$ S.D)	31.56 $\pm$ 7.57	32.36 $\pm$ 8.41	0.700

SD: standard deviation; CSU: chronic spontaneous urticaria.

et al.,<sup>28</sup> and Ayub et al.,<sup>29</sup> who noted a significant difference in the mean levels of serum TC, LDL-C, and HDL-C in CSU patients compared to controls.

On the contrary, our results regarding the statistically significant elevation of mean TG and insignificant elevation of HDL also stand in discordance with a study by Yaldiz and Asil et al.<sup>30</sup>

Statistically significantly elevated levels of mean serum TG and VLDL were noted among cases compared to controls in our study, enforcing the role of CSU in the development of dyslipidemia. Hence, it is better to evaluate patients with CSU for dyslipidemia, thereby preventing its dreadful complications and ultimately improving life expectancy.

### Limitations

The study is limited by its small sample size and the omission of BMI as a covariate.

### Conclusion

Dyslipidemia, involving particularly TG and VLDL, is more frequent in CSU patients and at a slightly younger age, and is often underreported because it is clinically asymptomatic, which can result in inadequate management and an elevated risk of atherosclerosis, cardiac, and cerebrovascular complications. Therefore, early detection and proper management can decrease the likelihood of subsequent complications and enhance the patient's quality of life.

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### Conflicts of interest

None.

### Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the ethics committee. SAGER guidelines have been followed as applicable 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 or creation of the content of this manuscript.







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# Pediatric herpes zoster in North Africa: clinical features and complications

## *Herpes zoster pediátrico no Norte de África: características clínicas e complicações*

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### Abstract

**Objective:** To characterize the clinico-epidemiological profile, complications, and outcomes of pediatric herpes zoster (HZ) at a North African tertiary center. **Method:** Retrospective review of children < 18 years with clinical HZ (unilateral dermatomal vesicular rash) from February 2016 to April 2025. **Results:** Twenty patients (M: F 1.86:1; mean age 7.13 ± 3.77 years). Most (85%) were immunocompetent; three had chemotherapy-treated malignancies. Pruritus predominated (50%), followed by pain (20%). Thoracic dermatomes were most common (55%), then trigeminal (30%; ocular involvement in 4). Acute complications affected 60%: bacterial superinfection (30%), zoster keratitis (20%). No neurological sequelae or post-herpetic neuralgia occurred. 95% received oral antivirals. Lesions resolved within two weeks, except one immunocompetent child with permanent dyschromic macules and hypertrophic scarring. **Conclusion:** Pediatric HZ mainly affects immunocompetent children in our setting and carries substantial acute complication risk, especially trigeminal. Early recognition and prompt antivirals are essential to minimize morbidity. Consider HZ in any child with dermatomal vesicular rash, irrespective of immune status.

**Keywords:** Complications. Herpes zoster. Immunocompetent. North Africa. Pediatric. Trigeminal.

### Resumo

**Objetivo:** Caracterizar o perfil clínico-epidemiológico, as complicações e os desfechos do herpes zoster (HZ) pediátrico num centro terciário do Norte de África. **Método:** Revisão retrospectiva de crianças < 18 anos com HZ clínico (erupção vesicular unilateral em dermatomas) de fevereiro de 2016 a abril de 2025. **Resultados:** Vinte doentes (M: F 1,86:1; idade média de 7.13 ± 3.77 anos). A maioria (85%) era imunocompetente; três tinham neoplasias malignas tratadas com quimioterapia. O prurido predominou (50%), seguido da dor (20%). Os dermatomas torácicos foram os mais comuns (55%), seguidos pelos trigêmeos (30%; envolvimento ocular em 4). As complicações agudas afetaram 60%: sobreinfecção bacteriana (30%), queratite por herpes zoster (20%). Não ocorreram sequelas neurológicas nem neuralgia pós-herpética. 95% receberam antivirais orais. As lesões desapareceram em duas semanas, exceto numa criança imunocompetente que apresentava máculas discrómicas permanentes e cicatrizes hipertróficas. **Conclusão:** O herpes zoster pediátrico afeta principalmente crianças imunocompetentes no nosso contexto e acarreta um risco substancial de complicações agudas, especialmente do trigêmeo. O reconhecimento precoce e o início imediato de antivirais são essenciais para minimizar a morbilidade. Considere o herpes zoster em qualquer criança com erupção vesicular dermatomal, independentemente do estado imunitário.

**Palavras-chave:** Complicações. Herpes zoster. Imunocompetente. Norte de África. Pediátrico. Trigêmeo.

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## Introduction

The Varicella-Zoster Virus (VZV), which causes chickenpox, belongs to the Herpesviridae family.<sup>1</sup> A hallmark of these viruses is their ability to establish latency, following primary infection or vaccination.<sup>2</sup> VZV persists in a dormant state within sensory neurons; declining VZV-specific cell-mediated immunity can trigger reactivation, resulting in herpes zoster (HZ).<sup>3</sup> The latter typically presents as a painful, unilateral dermatomal vesicular rash.<sup>4</sup> HZ is common in older adults, with an incidence of 3-5/1,000 person-years, rising sharply after age 50, and a recurrence rate of approximately 5%.<sup>5</sup> In contrast, HZ remains an uncommon cause of rash in children.<sup>6</sup> While traditionally associated with immunocompromised pediatric patients, recent reports have documented an increasing number of cases in otherwise healthy, immunocompetent children.<sup>7</sup> This retrospective case series aimed to describe the clinical characteristics, associated conditions, treatment approaches, and complications of HZ in children at our center, to promote early diagnosis and minimize complications.

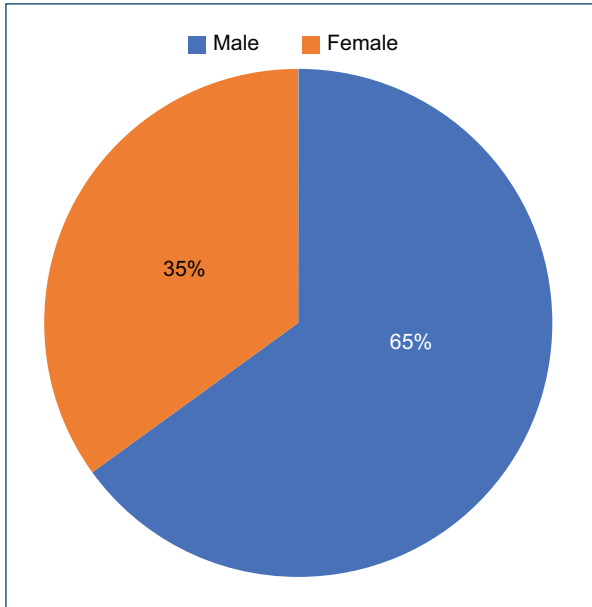
## Method

A retrospective observational study was conducted at the Dermatology Department of Hassan II University Hospital, Faculty of Medicine and Pharmacy, Sidi Mohamed Ben Abdellah University, Fez, Morocco. The study period extended from February 01, 2016, to April 30, 2025. Consecutive cases of pediatric HZ were identified by searching the hospital's electronic database using the keywords "herpes zoster" or "zona" in the diagnosis field. All children clinically diagnosed with HZ by a certified dermatologist were considered for inclusion. The clinical diagnosis was established based on a characteristic unilateral, dermatomal vesicular eruption, frequently accompanied by pain or dysesthesia; no PCR testing was performed or required, as the presentation was typical in these pediatric cases. Inclusion criteria were: (1) a clinical diagnosis of HZ and (2) age  $\leq$  18 years at the time of diagnosis. Exclusion criteria included patients aged  $>$  18 years or those with incomplete medical records regarding the studied variables (2 patients were excluded due to missing key data, such as follow-up until resolution or treatment details). Patient confidentiality was strictly maintained by anonymizing all personal identifiers during data entry. Written informed consent for the use of clinical photographs was obtained from parents or legal

guardians. Relevant data were extracted from patient files using a standardized, pre-tested data collection form. Collected variables included: demographic characteristics (age, sex), clinical features (involved dermatome, rash characteristics), medical history (previous chickenpox, varicella vaccination status, underlying immunosuppressive conditions), and treatment details (antiviral therapy, analgesics).

## Results

A total of 20 cases of HZ were managed in our department over a 9-year period. Sixty-five percent of patients ( $n = 13$ ) were male, and 35% ( $n = 7$ ) were female (Fig. 1), yielding a male-to-female ratio of 1.86. The mean age was  $7.13 \pm 3.77$  years, with a range from 11 months to 14 years. A documented history of varicella was present in 7 patients (35%). In 10 cases, there was no history of varicella, or the families could not recall an episode. Two children had been exposed to the VZV *in utero*, and one patient had a history of suspected close contact with varicella. Three patients had an underlying neoplastic disease and were receiving immunosuppressive chemotherapy at the onset of HZ. None of the patients had received the varicella vaccine. Pruritus was the most common symptom, reported by 10 patients (50%). Pain and burning sensations were present in 4 patients (20%), while 6 patients experienced a combination of pain, pruritus, and fever. The thoracic dermatomes were the most frequently involved (55% of cases) (Fig. 2), followed by trigeminal involvement (30%) (Fig. 3). Among the latter, four patients developed ocular complications. Cervical and lumbosacral dermatomes accounted for 10% and 5% of cases, respectively (Fig. 4). Oral mucosal involvement was observed in only one patient, limited to the right hard palate in a case of trigeminal (V2) HZ (Fig. 5). One 9-year-old child presented with involvement of the right external ear and cervical dermatomes but showed no clinical signs of 7<sup>th</sup> or 8<sup>th</sup> cranial nerve dysfunction. Identified predisposing factors included malignancy in 15% of patients (2 cases of leukemia and 1 of medulloblastoma), asthma in 1 patient, and significant stress reported in 4 patients. Regarding acute complications, bacterial superinfection was the most common (30%), followed by ocular involvement manifesting as zoster keratitis in 4 patients (20%) and stage 1 orbital cellulitis (preseptal) (per Chandler's classification) in 2 patients (10%). No neurological complications were recorded. All cases were diagnosed clinically based on detailed



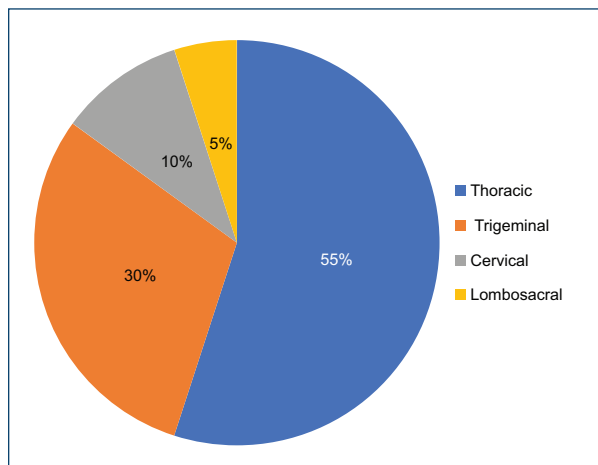
**Figure 1.** Out of 20 cases, 13 were males, 7 were females.



**Figure 3.** Ophthalmic shingles in a 10 year-old male child.



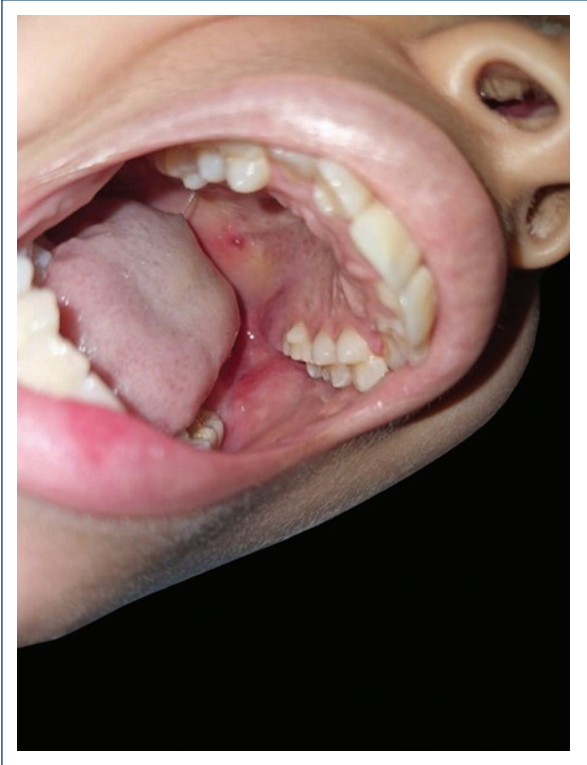
**Figure 2.** Intercostal shingles in an 11-year-old female child.



**Figure 4.** Site of involvement of herpes zoster.

history and typical physical findings. Laboratory tests were unremarkable except for mild leukocytosis in three patients and mild anemia in one. Twelve patients (60%) received oral valacyclovir (80 mg/kg/day divided every 6 h), seven (35%) received intravenous acyclovir

(20 mg/kg/day divided every 8 h), and one (5%) received symptomatic treatment only. All treated patients completed a 7- to 10-day course. The disease was self-limiting and resolved within two weeks in all but one case. One patient was left with a dyschromic macular patch and erythematous hypertrophic scarring (Fig. 6), which was subsequently managed with topical corticosteroids. Post-herpetic neuralgia was not observed in any patient during follow-up.



**Figure 5.** Oral mucosal involvement in a child with herpes zoster affecting the trigeminal dermatome.



**Figure 6.** Dyschromic macular patches and erythematous hypertrophic scarring in a 9-year-old boy, 6 months after resolution of herpes zoster involving the right cervical and trigeminal dermatomes.

## Discussion

HZ, from the Greek “zoster” meaning belt or girdle; also called shingles from the Latin “cingulum,”<sup>8</sup> has a generally low incidence in the pediatric population, with an estimated rate of 0.74 cases/1000 person-years, which is 4-7 times lower than in adults.<sup>9</sup> The incidence progressively increases with age, from 0.4 cases/1000 person-years in children between the ages of 1 and 9 years to 1.06 in the group of children > 10 years.<sup>9</sup> The primary risk factors for developing HZ in children are well-documented in the literature. These include maternal exposure to the VZV during pregnancy (with a risk of 0.8% for exposure at 13-24 weeks and 1.7% at 25-36 weeks).<sup>10</sup> Another significant factor is the timing of the primary varicella infection; contracting chickenpox within the 1<sup>st</sup> year of life carries a substantially higher risk, with an incidence of 410/100,000 person-years and a mean interval to zoster of 3.8 years, compared to 45/100,000 person-years and a mean interval of 6.2 years for infection after the 1<sup>st</sup> year.<sup>10</sup> Furthermore, immunocompromised states, such as malignancies, constitute a well-established risk factor, confer a 5-6 times higher risk due to cellular immunosuppression from the disease or its treatments (e.g., chemotherapy, radiotherapy).<sup>5,11</sup> Conditions,

such as asthma are associated with a two-fold increase in HZ risk.<sup>10</sup> In our cohort, some of these factors were observed: malignancy (15%), reported significant stress (20%), and asthma (5%). In addition, 35% had a documented history of varicella, and two children had been exposed to VZV *in utero*. The absence of classic immunosuppression in most of our patients underscores that HZ can develop in immunocompetent children. The mean age in our study was  $7.13 \pm 3.77$  years (range: 11 months-14 years), indicating a predominance in school-age children, with a male predominance, this aligns with a Turkish study of 60 pediatric HZ cases, which reported a mean age of  $8 \pm 4.93$  years and a male predominance (37 boys vs. 23 girls).<sup>7</sup> Diagnosis is primarily clinical, characterized by a painful, erythematous, maculopapular rash that rapidly progresses, within a single dermatome and without crossing the midline, to clear-fluid-filled vesicles, which subsequently become pustular and then crust over.<sup>12</sup> Unlike in adults, where pain predominates, itching is the most common symptom in children, followed by pain, fever, and weakness.<sup>13</sup> Our findings are consistent with pruritus reported in 50% of cases. Thoracic dermatomes are most frequently involved in children,<sup>7,8,14</sup> a pattern reflected in our series (55% of cases),

followed by trigeminal, cervical, and lumbosacral involvement. Although generally self-limiting, systemic antiviral therapy is indicated for immunodeficiency, disseminated disease, or ophthalmic involvement (especially with nasociliary branch involvement).<sup>10</sup> Treatment may also be considered for otherwise healthy children to prevent scarring, ocular complications, and acute pain.<sup>15</sup> Early initiation (within 72 h of rash onset) for at least 7 days accelerates healing and reduces complications,<sup>8,12,16</sup> as applied in our case series. Potential complications include secondary bacterial infection, ocular involvement, neurological sequelae, and scarring.<sup>4</sup> In our series, acute complications occurred in 60% of patients, most commonly secondary bacterial superinfection (30%) and keratitis (20%, all with trigeminal involvement). No neurological complications or post-herpetic neuralgia were observed, consistent with other pediatric studies.<sup>7,17</sup> One patient developed permanent dyschromic macules and hypertrophic scarring.

## Conclusion

HZ is an uncommon, generally self-limited condition in children, typically characterized more by pruritus than by pain, and carries a minimal risk of post-herpetic neuralgia. Nevertheless, complications, such as bacterial superinfection and ocular involvement necessitate close monitoring. Importantly, our study revealed that most affected children were immunocompetent, highlighting that HZ can occur without classic risk factors or underlying immunodeficiency. Consequently, HZ should be considered in any child presenting with a dermatomal vesicular rash. Early recognition and prompt antiviral therapy remain the cornerstone to prevent morbidity.

## Funding

None.

## Conflicts of interest

None.

## Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable 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 or creation of the content of this manuscript.

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## Pigment meets vascularity: dermoscopic patterns of port-wine stains in fitzpatrick skin type IV and V – insights from a tertiary care center in Eastern India

*Pigmento encontra vascularidade: padrões dermatoscópicos do vinho do porto em tipos de Pele IV e V de fitzpatrick – percepções de um centro de cuidados terciários no Leste da Índia*

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### Abstract

**Objectives:** Port-wine stain (PWS) or nevus flammeus, a benign congenital capillary malformation characterized by an erythematous macule to plaque that often darkens and hypertrophies over time. While dermoscopy has emerged as a non-invasive modality for assessing vascular morphology in dermatology, limited data exist to describe dermoscopic features of PWS in Indian patients with Fitzpatrick skin types IV and V and explore morphological correlations with age. **Methods:** Seventeen patients with PWS aged between 6 and 34 years were enrolled in the study. Each patient underwent dermoscopic evaluation, and vascular morphology was noted. **Results:** Majority of the patients had lesions over the head-and-neck region (76.47%). Dermoscopy revealed dots and clots to be the most common finding present in 100% of the cases, followed by linear vessels in 94.11% and sausage vessels in 23.52%. Reticulate hyperpigmentation (88.23%) and white veil (41.17%) were the most common non-vascular features. **Conclusion:** This study demonstrates the utility of dermoscopy in identifying vascular morphologies of PWS in Indian patients. The predominance of dots and globules in the younger age group and the emergence of linear or mixed vessels in older patients align with findings by Huang et al. and Ngoc et al. Despite the study's limitations of lacking histological confirmation, these findings contribute novel insights into PWS evaluation in darker skin types.

**Keywords:** Port-wine stain. Dermoscopy. Fitzpatrick skin type. Dots and globules. Mixed vessels.

### Resumo

**Objetivos:** A mancha vinho do porto (PWS) ou nevo flâmneo é uma malformação capilar congênita benigna, caracterizada por máculas eritematosas que podem evoluir para placas, frequentemente escurecendo e apresentando hipertrofia ao longo do tempo. Embora a dermatoscopia tenha emergido como uma modalidade não invasiva para a avaliação da morfologia vascular em dermatologia, existem dados limitados que descrevam as características dermatoscópicas do PWS em pacientes indianos com fototipos cutâneos IV e V de Fitzpatrick, bem como que explorem as correlações morfológicas com a idade. **Métodos:** Dezessete pacientes, com idades entre 6 e 34 anos, participaram do estudo. Cada paciente foi submetido à avaliação dermatoscópica, e a morfologia vascular foi registrada. **Resultados:** A maioria dos pacientes apresentou lesões na

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região da cabeça e do pescoço (76.47%). A dermatoscopia revelou pontos e glóbulos como os achados mais comuns, presentes em 100% dos casos, seguidos por vasos lineares em 94.11% e vasos em forma de salsicha em 23.52%. Entre as características não vasculares, a hiperpigmentação reticulada (88.23%) e o véu branco (41.17%) foram as mais frequentes.

**Conclusão:** Este estudo demonstra a utilidade da dermatoscopia na identificação das morfologias vasculares do PWS em pacientes indianos. A predominância de pontos e glóbulos em grupos etários mais jovens e o surgimento de vasos lineares ou mistos em pacientes mais velhos estão de acordo com os achados de Huang et al. e Ngoc et al. Apesar da limitação do estudo pela ausência de confirmação histológica, esses resultados contribuem com novas percepções sobre a avaliação do PWS em tipos de pele mais escuros.

**Palavras-chave:** Mancha vinho do porto. Dermatoscopia. Fototipo de Fitzpatrick. Pontos e glóbulos. Vasos mistos.

## Introduction

Port-wine stains (PWS), also known as nevus flammeus represents a dermal capillary hamartomatous malformation and are the most common benign congenital capillary malformation. Its prevalence is reported to be 0.3-1%, with females being affected twice as often as males.<sup>1</sup> It clinically presents as a well-defined unilateral, bilateral, or centrally placed pink to red patch that is present at the time of birth. It persists throughout life and progressively darkens in later life, and can potentially form nodules or hypertrophic plaques in adulthood. It can be localized in any part of the body but has a predilection for the head and neck.<sup>2</sup>

Cases are usually sporadic, but in 10% of the cases, familial incidence and an autosomal dominant inheritance have been described.<sup>3</sup> PWS can be part of syndromes such as Sturge-Weber syndrome, a nonfamilial congenital disease with ocular and intracranial complications or neurological deficits, or Klippel-Trenaunay Syndrome with limb overgrowth.

Acquired port-wine stains are rarely observed, often reported in adolescents or adults, usually following trauma. They are clinically and histopathologically indistinguishable from congenital capillary malformation.

Dermoscopy has emerged as a valuable tool for evaluating vascular morphology non-invasively, contributing both to the diagnosis and treatment planning. Although dermoscopy has been used in the evaluation of PWS, there are limited data on its application in Indian populations. This case series of 17 patients from eastern India highlights distinct dermoscopic features in the skin of higher phototypes, with possible implications for diagnosis and lesion monitoring. In addition, we explore correlations with lesion site and morphology, contributing novel insights to the existing literature.

## Methods

A prospective observational analysis was conducted at dermatology outpatient department of a tertiary care center in eastern India over 12 months (March 2024-March 2025). Seventeen patients with clinically diagnosed PWS were included in the study after giving their informed consent or their guardian's consent.

Clinical data, including age, sex, lesion site, and brief history, were noted. Each patient underwent a clinical examination followed by dermoscopic evaluation using non-polarized DermLite DL5 dermoscope. Images were recorded using an iPhone 15, focusing uniformly over central most region of the PWS. Vascular morphology, as well as other relevant dermoscopic findings, were recorded and correlated with lesional age and localization.

## Results

Seventeen patients with PWS, 6 males and 11 females (male-to-female ratio 2:3), were analyzed in this series. Patients' age ranged from 6 to 34 years (mean  $17.6 \pm 8.7$  years). Within this group, 13 (76.47%) patients presented with PWS on the head-and-neck region (Fig. 1); two (11.76%) patients had involvement of the lower limb, and two (11.76%) patients the upper limb. Among these, one (5.88%) patient also had tongue involvement, and another had developed a  $0.5 \times 0.5$  cm soft nodule over the PWS on the trunk at the age of 32 years (Fig. 2 and Table 1). All the lesions were present at birth, and all the patients were asymptomatic, with the sole complaint being a cosmetic concern.

Dermoscopic evaluation revealed a varied vascular morphology, with the most common finding being dots and globules observed in all patients (100%). In addition, linear vessels were present in 16 cases of PWS (94.11%) and sausage-shaped vessels in four (23.52 %) (Fig. 3). Two most observed non-vascular characteristics were white veil and reticulate

**Table 1.** Age distribution of patients, localization of port-wine stain, fitzpatrick skin type and dermoscopic findings

Age group	Location	Fitzpatrick skin type	Dermoscopic findings	
			Background	Vessel morphology
5-10 (n = 4)	Face	V (n = 4)	Red-white background	Dots, globules, reticular arrangement
11-15 (n = 6)	Face	IV (n = 1), V (n = 5)	Red-white background	Dots, globules
16-20 (n = 3)	Face, dorsum of foot, tongue	IV (n = 1), V (n = 2)	Red-white background	Dots, globules, linear vessels
21-25 (n = 1)	Dorsum of foot	V (n = 1)	Brown background	Dots, globules
26-30 (n = 0)	-	-	-	-
31-35 (n = 3)	Trunk, upper limb	V (n = 3)	Brown background	Dots, globules, sausage vessels, nodule

**Figure 1.** Clinical image of port-wine stain over left aspect of face disturbed over nose, malar region and left zygomatic arch taken by iPhone 15.

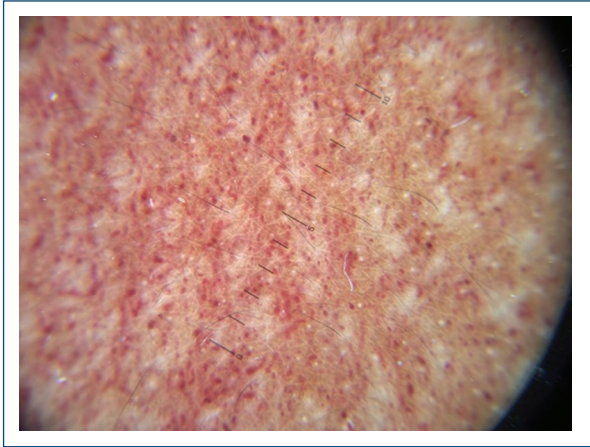
hyperpigmentation, the latter being twice as common as the former, mostly seen in PWS involving the face. One patient (5.88%) had a globular nodule over a background of PWS (Fig. 4). With increasing age, findings progressed from red-white background with superficial vascular patterns, mainly dots and globules, to brown background along with emergence of sausage-shaped vessels and nodular changes in the

**Figure 2.** Clinical image of nodule over background of port-wine stain over trunk taken by iPhone 15.

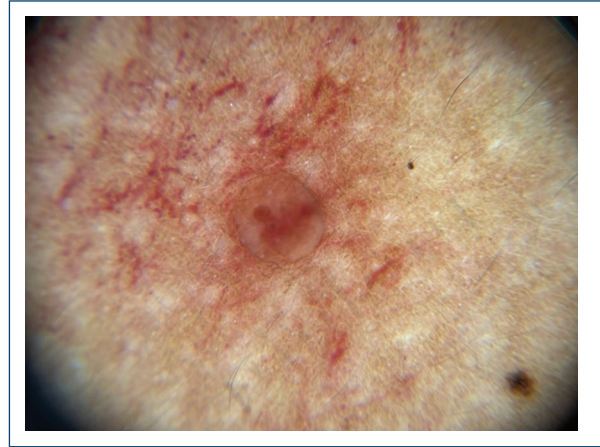
higher age group. Table 1 summarizes the demographic data, location of PWS, skin type, and their dermoscopic findings.

## Discussion

Port-wine stains are congenital vascular malformations characterized by ectatic dermal blood vessels that appear at birth and persist throughout life, often progressing in color and surface morphology over time. The treatment includes vascular targeting lasers such as intense pulsed light (IPL), pulsed dye laser (PDL), and recently also photodynamic therapy. Dermoscopy is a useful tool in evaluating various dermatological conditions involving blood vessel abnormalities, and, in the case of PWS, it may contribute to predict therapy response.



**Figure 3.** Dermoscopic image obtained using DermLite DL5 dermoscope at  $\times 10$  magnification depicting dots, globules, linear vessels and sausage vessels.



**Figure 4.** Dermoscopic image of nodule over background of port-wine stain at  $\times 10$  magnification visualized through DermLite DL5 dermoscope.

**Table 2.** Comparison of our study with Huang et al.<sup>4</sup> and Ngoc et al.<sup>6</sup>

Dermoscopic feature	n = 17 (%)	Huang et al. n = 264 (%)	Ngoc et al. n = 148 (%)
Dots and globules	17 (100)	9.10	76.40
Linear vessels	16 (94.11)	42.00	68.90
Whitish veil	7 (41.17)	38.30	29.10
Reticular hyperpigmentation	15 (88.23)	-	-
Mixed vessels	4 (26.66)	19 (7.2)	47 (31.8)

The capillaroscopic pattern of PWS can be divided into Type I (dots or globules which represent vertical capillaries located in the papillary dermis), Type II (linear vessels and reticular vessels representing horizontal capillaries in the reticular dermis),<sup>4</sup> and Type III (mixed vessels that exhibit combined features of both Type I and Type II capillaroscopic pattern).<sup>5</sup> Our series offers an insight into dermatological patterns of PWS. The presence of dots and globules was the most common finding, more prevalent in the younger age group, aligning with the findings of Ngoc et al.<sup>6</sup> Linear vessel pattern was the second most common vascular morphology in our study, also in agreement with Ngoc et al., while Huang et al. found it to be the most common pattern. Mixed vessel pattern was seen in lower frequency and in the older age group, mirroring the associations reported by Huang et al. with chronicity.<sup>5</sup> Looped vessels or sausage-shaped vessel and complications such as nodule formation were reported in thicker and more hypertrophic PWS.<sup>5</sup> Minkis et al.

reported that approximately 65% of PWS become hypertrophic or nodular by the fifth decade of life, indicating PWS do not involute spontaneously, but rather tend to evolve over time.<sup>7</sup> Table 2 compares the various dermoscopic findings seen in our series with those of Huang et al.<sup>4</sup> and Ngoc et al.<sup>6</sup>

The relevance of these dermoscopic vascular patterns extends beyond morphological classification and has implications for response to laser therapy. Prior histopathological and laser response studies have demonstrated that vessel depth and diameter are critical determinants of laser efficacy<sup>8</sup>. Shirakawa et al. emphasized that superficial vessels show a better response to laser therapy, while treatment efficacy diminishes as vessels become deeper. Vessel diameter also plays a key role: larger, superficial vessels respond more favorably to laser treatment compared with smaller diameter vessels located deeper in the dermis. These findings suggest that dermoscopic patterns dominated by dots and globules representing superficial papillary dermal vessels are more amenable to PDL or IPL therapy<sup>9</sup>. In addition, laser therapy for PWS may be less effective in individuals with higher Fitzpatrick skin types due to higher epidermal melanin, which limits energy penetration, thereby influencing treatment outcomes despite having favorable dermoscopic vascular patterns.<sup>10</sup>

Bhagwat et al. studied the utility of dermoscopy in pediatric vascular anomalies, in which they recruited 61 patients below 18 years of age. Out of 61, 8 presented with PWS, where the dermoscopic findings were classified as dots, globules, and a broken

network of thick and/or thin vessels. They emphasized the reticular arrangement pattern, which was not visualized in our study due to the lesser magnification as compared to the video dermoscopy used in their study.<sup>11</sup>

Limitations of our study included the small number of patients studied, which did not allow for a good correlation of dermoscopic parameters with age or localization of the lesion. Furthermore, as treatment was not evaluated, we could not confirm the utility of dermoscopy as a predictor of treatment response.

Although various case series on dermoscopy of PWS exist, findings in Indian skin have not been evaluated before. Our case series highlights the utility of dermoscopy in the correct diagnosis. Dots, globules, and linear vessels are more favorable indicators occurring in the younger age group, while mixed patterns occur over time.

Our case series highlights the utility of dermoscopy in diagnosis but also as a potential prognostic adjunct in PWS. Dots, globules, and linear vessels are more favorable indicators reflecting their association with earlier disease stage and their known responsiveness to treatment, while mixed patterns occur over time. Dermoscopic identification of superficial vascular patterns may help anticipate treatment response and guide patient counseling.

## 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 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 artificial intelligence was used in the writing of this manuscript for the translation of the abstract section from English to Portuguese.

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# Herpes simplex lymphadenitis in an immunocompetent patient: diagnostic pitfalls on cytology and review of literature

*Linfadenite por herpes simplex em um paciente imunocompetente: armadilhas diagnósticas na citologia e revisão da literatura*

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## Abstract

Herpes simplex virus (HSV) lymphadenitis is an uncommon manifestation in immunocompetent individuals and is rarely seen as an isolated presentation. This report describes the case of a 23-year-old immunocompetent female who presented with inguinal lymphadenopathy and a painful labial rash. Fine-needle aspiration cytology of the inguinal lymph node revealed an inflammatory background with multinucleated giant cells, ground-glass nuclei, and occasional intranuclear inclusions. Immunohistochemistry confirmed HSV type 2 infection, which was supported by serological positivity. The patient responded well to acyclovir therapy, with complete resolution and no recurrence at 6-month follow-up. HSV lymphadenitis may mimic other viral or granulomatous infections histologically, making cytomorphologic recognition crucial. Thus, HSV should be considered in the differential diagnosis of lymphadenopathy and a detailed hematologic and immunologic workup should be done due to its known association with hematologic malignancies.

**Keywords:** Herpes simplex. Lymphadenitis. Cytology.

## Resumo

A linfadenite por vírus herpes simplex (HSV) é uma manifestação incomum em indivíduos imunocompetentes e raramente é vista como uma apresentação isolada. Este relato descreve o caso de uma mulher de 23 anos, imunocompetente, que apresentou linfadenopatia inguinal e exantema labial doloroso. A citologia aspirativa por agulha fina (PAAF) do linfonodo inguinal revelou um fundo inflamatório com células gigantes multinucleadas, núcleos em vidro fosco e inclusões intranucleares ocasionais. A imuno-histoquímica confirmou infecção por HSV tipo 2, corroborada pela positividade sorológica. A paciente respondeu bem à terapia com aciclovir, com resolução completa e sem recorrência no acompanhamento de seis meses. A linfadenite por HSV pode mimetizar histologicamente outras infecções virais ou granulomatosas, tornando o reconhecimento citomorfológico crucial. Portanto, o HSV deve ser considerado no diagnóstico diferencial de linfadenopatia e uma investigação hematológica e imunológica detalhada deve ser realizada devido à sua conhecida associação com neoplasias hematológicas.

**Palavras-chave:** Herpes simplex. Linfadenite. Citologia.

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## Introduction

Herpes simplex virus (HSV) infection commonly involves skin, mucous membranes, eye, and central nervous system. Out of the two serologic types of HSV, HSV2 is more commonly associated with genital herpes. Lymphadenitis is a rare complication of HSV and can occur as a part of a systemic HSV involvement or associated with skin rash.<sup>1</sup> Rarely, isolated lymphadenitis without any other evidence of HSV infection can also occur. Microscopic findings and correlation with serology becomes very important in these cases. Although histopathological features of HSV lymphadenitis are well documented, literature on cytomorphological features is scarce.<sup>2,3</sup> We describe the cytology findings of HSV lymphadenitis in a young immunocompetent female with inguinal lymphadenopathy and vulvar lesions.

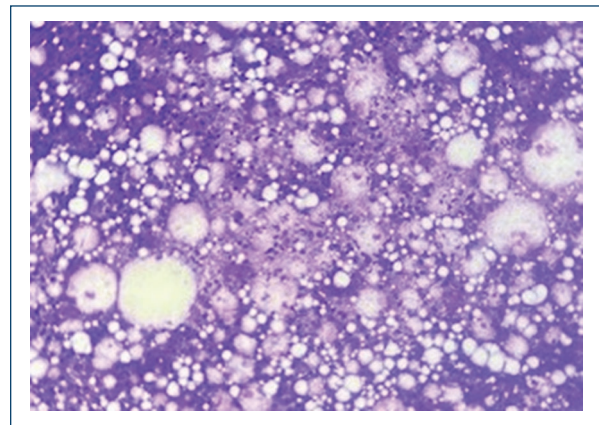
## Case report

A 23-year-old woman presented with a swelling in the groin region for the past 3 weeks. It was gradually progressive, associated with dull ache and on and off fever. On examination, a firm, fixed, non-tender lymph node (LN) of 2 × 1.5 cm was palpable in the inguinal region along with an erythematous painful non-ulcerated lesion on the labia majora (Fig. 1). There were no other vulvar or vaginal lesions. She had had no treatment before and her past medical history revealed only an episode of Bell's palsy 8 months beforehand that resolved in 4 months. The patient was sexually active and in a monogamous relationship for the past 3 years.

Fine-needle aspiration (FNA) from the inguinal LN yielded purulent material. FNA smears showed an inflammatory background consisting of neutrophils, many histiocytes, and multinucleated giant cells and occasional mononuclear cells with ground glass nuclei and occasional intranuclear inclusion (Figs. 2 and 3). A cell block was also made and immunohistochemistry (IHC) with HSV1 and 2 was performed. The cells showed nuclear immunoreactivity with HSV2. Serology with HSV also came positive (Fig. 4). Viral serology for human immunodeficiency virus, hepatitis B virus, and hepatitis C virus was also done and came to be negative. Thus, a final diagnosis of HSV lymphadenitis was rendered. Complete blood count revealed normal findings. The patient received acyclovir for 10 days following which the swelling disappeared. At 6 months of follow-up, the patient is doing well and is free of recurrence.



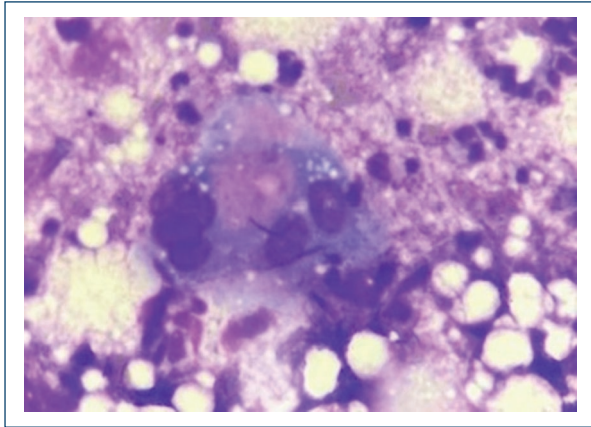
**Figure 1.** Clinical picture showing inguinal lymph node measuring 2 × 1.5 cm.



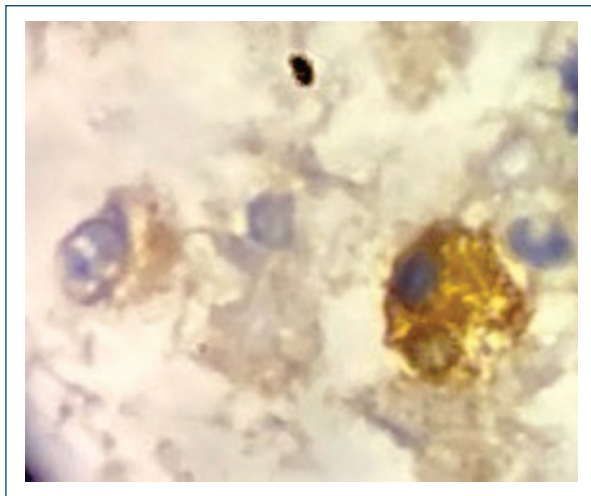
**Figure 2.** Fine-needle aspiration smear showing necroinflammatory background with neutrophils, histiocytes, binucleate histiocytes, and lymphocytes. Giemsa: ×200.

## Discussion

HSV has two serologic types: HSV1 and HSV2. Genital infection is more commonly seen with HSV2 and non-genital involvement with HSV1; however, overlap is seen.<sup>1</sup> HSV is a deoxyribonucleic acid (DNA) virus with the ability to establish latent infection, which might get reactivated and disseminated in case of immunocompromised state. Isolated lymphadenopathy in HSV infection with or without associated mucocutaneous involvement is rarely seen, especially in immunocompetent host. Although HSV infection runs an indolent and self-limited course, HSV lymphadenitis



**Figure 3.** Fine-needle aspiration smear showing necroinflammatory background with multinucleated giant cell showing multinucleation, molding, and ground glass nuclei with occasional intra-nuclear inclusion. Giemsa: x400.



**Figure 4.** Nuclear positivity with herpes simplex virus 2 antigen x1000.

needs to be diagnosed timely due to its well-documented association with hematologic malignancies. In a review of 27 cases of HSV lymphadenitis by Robertson et al.,<sup>4</sup> 11 out of 27 cases were immunocompetent while 16 had comorbidities that included lymphomas (10), leukemias (one acute myelocytic leukemia and one chronic myelocytic leukemia), steroid therapy (2), and immunodeficiency disorders (2). Out of these, HSV is more commonly associated with chronic lymphocytic leukemia. Inguinal LNs were most commonly involved followed by cervical. Cases of hematologic malignancies developing after their diagnosis of HSV

lymphadenitis have also been reported.<sup>5</sup> Thus, diagnosis of HSV lymphadenitis also warrants a hematologic work up as well as follow-up of the patient.

Various histomorphological features observed in HSV lymphadenitis include prominent paracortical expansion, follicular hyperplasia, dilated sinusoids filled with histiocytes, lymphocytes, and immunoblasts and monocytoid B-cell hyperplasia and often variable necrotic areas with neutrophils, karyorrhexic nuclear material, and smudged eosinophilic cellular ghosts of necrotic cells.<sup>6</sup> Cells with viral cytopathic effects such as “ground-glass” nuclei, viral-like inclusions, and multinucleated giant cells can also be observed as well as necrotizing granulomatous inflammation.<sup>7</sup> However, many of these features overlap with those seen in viral lymphadenopathies such as cytomegalovirus and Epstein-Barr virus. If HSV is associated with necrotizing granulomatous inflammation, tuberculosis, fungi, atypical mycobacteria, Yersinia, lymphogranuloma venereum, and cat-scratch disease need to be ruled out. Necrosis with karyorrhectic bodies along with prominence of phagocytic mononuclear cells also gives rise to the differential of Kikuchi’s disease. Thus, demonstration of HSV by serological studies, IHC or DNA hybridization, is essential in definitive diagnosis. Cytopathological findings include balloon like nuclear degeneration, margination of nuclear chromatin along the nuclear membranes, ground glass nuclei, intranuclear eosinophilic inclusion bodies, and cells with bi, tri, and multinucleation with nuclei lined in private soldier such as pattern and mosaic arrangement.<sup>2,3</sup> The background is necrotic and inflammatory. In the present case, fine-needle aspiration cytology findings included necrosis, multinucleated giant cells, nuclear margination, and ground glass nuclei.

HSV leads an indolent course and is a self-limited disease. Treatment with acyclovir is well tolerated. HSV lymphadenitis is relatively rare, even in the setting of generalized HSV infection. HSV should be considered in the differential diagnosis of inguinal lymphadenopathy, especially when the LN is tender. HSV lymphadenitis should prompt a complete hematologic and immunologic work up of the patient.

## Funding

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## Conflicts of interest

None.

## Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable 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 or creation of the content of this manuscript.

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## Dermoscopy as a significant tool for diagnosing an exuberant case of HIV-associated pityriasis lichenoides et varioliformis acuta

*Dermatoscopia como ferramenta importante no diagnóstico de caso exuberante de pitiríase liquenoide e varioliforme aguda associado ao HIV*

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### Abstract

Pityriasis lichenoides et varioliformis acuta (PLEVA) is a rare dermatological condition of uncertain etiology characterized by polymorphic and often exuberant skin lesions. The use of dermoscopy has been successfully applied for the early diagnosis of this pathology, as well as in distinguishing it from other potential differential diagnoses. In this study, we present the dermoscopic features observed in a severe case of human immunodeficiency virus-associated PLEVA, which are consistent with those previously described in the literature. Furthermore, we describe a dermoscopic pattern that has not yet been reported in the studies published to date. Dermoscopy is an excellent diagnostic tool that aids in the early detection and accurate characterization of skin lesions. Therefore, knowledge of the dermoscopic patterns of this disease is essential to improve early suspicion and diagnostic accuracy.

**Keywords:** PLEVA. HIV. Dermoscopy.

### Resumo

Pitiríase Liquenoide e Varioliforme Aguda (PLEVA) é uma afecção dermatológica rara, de etiologia ainda não completamente esclarecida, caracterizada pelo aparecimento de lesões cutâneas exuberantes nos indivíduos acometidos. A dermatoscopia tem se mostrado uma ferramenta valiosa no diagnóstico precoce dessa condição, além de contribuir para a sua diferenciação em relação a outras dermatoses de apresentação clínica semelhante. Neste relato, descrevemos as características dermatoscópicas observadas em um caso exuberante de PLEVA associado à infecção pelo HIV, as quais são compatíveis com aquelas previamente descritas na literatura. Além disso, relatamos um padrão dermatoscópico ainda não documentado em publicações anteriores. A dermatoscopia constitui um instrumento diagnóstico de grande utilidade, por permitir a identificação precoce e a caracterização detalhada das lesões cutâneas. Assim, o conhecimento dos padrões dermatoscópicos característicos da PLEVA é fundamental para aumentar o grau de suspeição clínica e favorecer o diagnóstico precoce dessa enfermidade.

**Palavras-chave:** PLEVA. HIV. Dermatoscopia.

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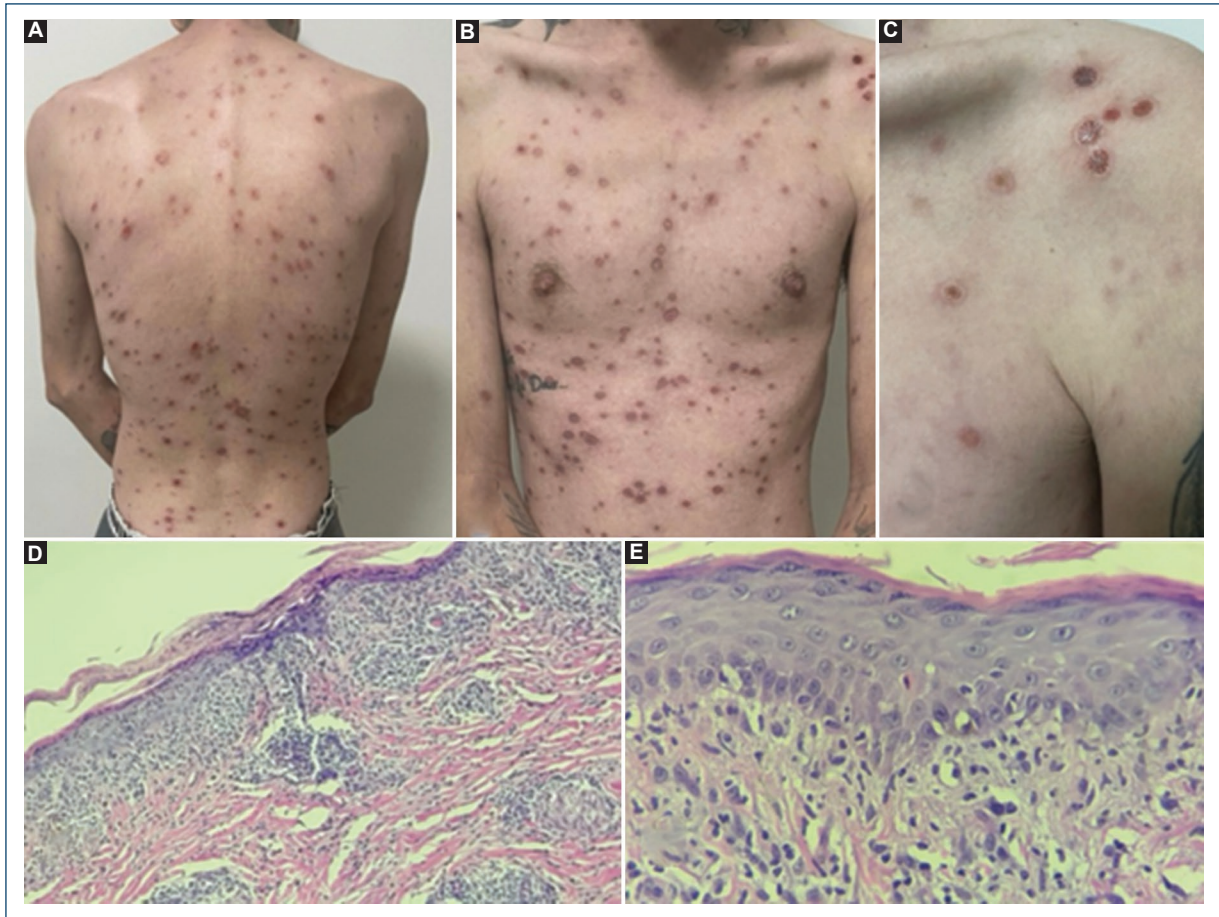
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**Figure 1.** Clinical and histopathological features of the lesions. **A-C:** multiple erythematous-violaceous macules and papules, some with an ulceronecrotic surface, predominantly located on the upper limbs and trunk. Note the lesions in different stages of progression in C. **D and E:** histopathological findings showing a horizontal band infiltrate at the dermoepidermal junction, perivascular infiltration, parakeratosis, exocytosis of lymphocytes and neutrophils into the stratum corneum, forming corneal microabscesses.

## Introduction

Pityriasis lichenoides et varioliformis acuta (PLEVA) is a rare dermatological condition of uncertain etiology, predominantly affecting young adults. Proposed triggers include medication use, vaccinations, and inflammatory responses to infectious agents, notably the human immunodeficiency virus (HIV).<sup>1</sup>

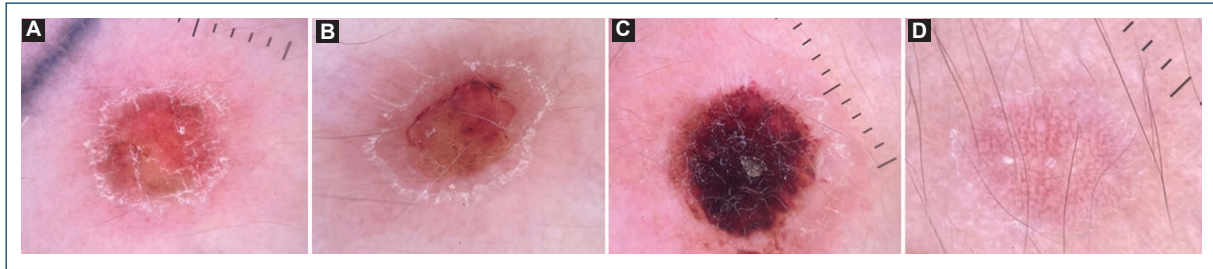
Clinically, PLEVA manifests as the sudden onset of multiple erythematous macules that progress into pustules or vesicles containing hemorrhagic fluid, often culminating in central ulcerations. Systemic symptoms can be present or absent alongside dermatological presentation.<sup>2,3</sup> Diagnosis relies on clinical assessment corroborated by histopathological findings.<sup>4</sup> However, histopathological examination may not be immediately available in all clinical settings, highlighting the importance of a noninvasive

diagnostic tool. Dermoscopy is an invaluable tool in the early diagnosis of this condition, offering distinct features that aid in differential diagnosis.<sup>2,5</sup> We present a case of HIV-associated PLEVA, confirmed through histopathology, with an exuberant presentation of lesions displaying dermoscopic features consistent with the condition.

## Case report

A 27-year-old male patient with a confirmed HIV diagnosis presented with a 3-week history of sudden onset erythematous macules evolving into papules and plaques with ulceronecrotic surfaces. The lesions predominantly affected the trunk and upper limbs (Fig. 1A-C).

Dermoscopy was performed using a polarized handheld dermatoscope at  $\times 10$  magnification and revealed



**Figure 2.** Dermoscopic features of the lesions. **A** and **B**: target-like pattern formed by a peripheral vascular outer ring followed by intermediate white scales and a center with a yellow-brownish mass. **C**: center formed by a hematinic crust, followed by a subtle peripheral white scale, surrounded by a slight erythematous halo. **D**: discreet erythematous vascular halo and thin circular white scale, encircling a vascular network composed of irregular linear vessels, occasionally forming vascular loops.

distinct morphological patterns. The most characteristic was target-like lesions composed of a peripheral vascular ring, intermediate white scales, and a red-brown central area (Figs. 2A and B). Additional findings included lesions with a central hematic crust, surrounded by white peripheral scaling and a faint erythematous halo (Fig. 2C). The third most observed pattern consisted of lesions with minimal or absent erythematous halos, fine circular white scaling, and a vascular network of irregular linear vessels occasionally forming vascular loops (Fig. 2D).

Histopathology confirmed the diagnosis of PLEVA, demonstrating a vacuolar interface dermatitis with features such as parakeratosis, lymphocytic and neutrophilic exocytosis, and the formation of corneal microabscesses (Figs. 1D and E).

## Conclusion

Dermoscopy represents a valuable adjunctive diagnostic tool in cases of PLEVA, facilitating differentiation from clinically similar conditions such as viral exanthems, varicella, and guttate psoriasis.<sup>5</sup> The dermoscopic findings observed in our patient are largely consistent with those previously described in the literature, including the well-established target-like pattern considered pathognomonic by several authors. In addition, we describe a dermoscopic presentation not previously reported, characterized by a central vascular pattern composed of tortuous linear vessels. These observations reinforce the relevance of dermoscopy as a rapid, noninvasive bedside tool. Further studies are warranted to better characterize dermoscopic patterns of PLEVA and to support the development of standardized diagnostic criteria.

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## Conflicts of interest

The authors declare no conflicts of interest.

## Ethical considerations

**Protection of human subjects and animals.** The authors declare that no experiments on humans or animals were performed 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 or creation of the content of this manuscript.

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# Achenbach syndrome: a benign cause of blue finger illustrated by a case report

*Síndrome de Achenbach: uma causa benigna de dedo azul a propósito de um caso clínico*

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## Abstract

Achenbach syndrome, or paroxysmal finger hematoma, is a benign vascular condition characterized by the sudden onset of pain, swelling, and bluish discoloration of the digits. Although self-limited, its dramatic presentation often leads to unnecessary investigations to exclude ischemic or thrombotic disease. We present a case of a 48-year-old female with acute-onset discoloration of the third finger and full spontaneous resolution within 1 week, illustrating the importance of recognizing this frequently underdiagnosed syndrome.

**Keywords:** Achenbach syndrome. Paroxysmal finger hematoma. Blue finger.

## Resumo

A síndrome de Achenbach, ou hematoma digital paroxístico, é uma condição vascular benigna e frequentemente subdiagnosticada, caracterizada pelo aparecimento súbito de dor, edema e descoloração azulada de um ou mais dedos. Apesar do seu curso autolimitado, a apresentação clínica pode ser alarmante e levar à realização de exames desnecessários para excluir patologia isquémica ou trombótica. Descrevemos o caso de uma mulher de 48 anos com descoloração violácea de início abrupto no terceiro dedo da mão esquerda, com resolução completa ao fim de uma semana. Este caso ilustra as características clínicas típicas, os principais diagnósticos diferenciais e reforça a importância do reconhecimento desta entidade, de modo a evitar procedimentos invasivos e a reduzir a ansiedade dos doentes.

**Palavras-chave:** Síndrome de Achenbach. Hematoma digital paroxístico. Dedo azul.

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## Introduction

Achenbach syndrome, first described in 1958 by Walter Achenbach, is a benign and self-limited vascular condition characterized by sudden-onset subcutaneous bleeding of the fingers, most frequently affecting middle-aged women.<sup>1</sup> Although its exact pathophysiology remains unclear, proposed mechanisms include capillary fragility, microhemorrhages, vasomotor instability, and a possible genetic predisposition.<sup>2,3</sup> Despite its harmless course, its abrupt and dramatic clinical presentation often raises concern for more serious vascular disorders such as acute digital ischemia, vasculitis, or thromboembolic events, frequently prompting extensive investigations.<sup>3,4</sup> Improving clinical awareness allows clinicians to recognize this entity promptly, avoid unnecessary diagnostic workup, and reduce patient anxiety.

## Case report

A 48-year-old woman presented with a sudden-onset violaceous discoloration of the third finger of her left hand. Symptoms developed over several hours without preceding trauma, cold exposure, medication changes, or systemic complaints. Clinical examination revealed violaceous discoloration and mild oedema localized to the palmar aspect of the middle phalanx, with sparing of the fingertip and nail bed (Fig. 1). Radial and ulnar pulses were intact, and Allen's test was normal. Sensory and motor examination was unremarkable.

Laboratory investigations, including complete blood count, coagulation profile, and inflammatory markers, were unremarkable. Given the characteristic presentation and absence of red flags, no imaging was performed.

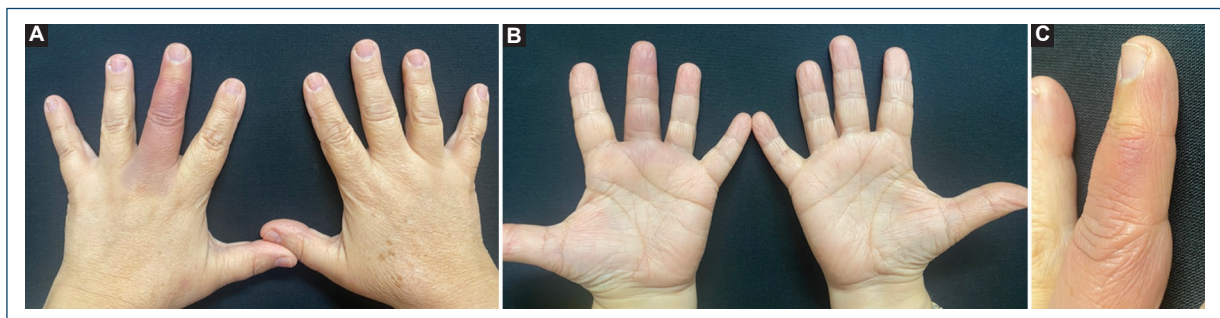
The patient was reassured, and symptoms resolved spontaneously within 7 days without intervention.

## Discussion

Achenbach syndrome is a benign vascular phenomenon characterized by acute-onset pain, swelling, and bluish discoloration of one or more fingers.<sup>1,3,5,6</sup> It most frequently involves the index, middle, or ring fingers, particularly the proximal and middle phalanges, classically sparing the fingertip.<sup>5-7</sup> Associated symptoms may include paresthesia, pruritus, or transient stiffness, but systemic signs are absent.

Although its etiology remains incompletely understood, the most accepted hypotheses involve increased vascular fragility and microhemorrhages within the dermis.<sup>2,5,7,8</sup> Some authors suggest a potential role for vasospasm, hematoma-induced compression, or subtle arterial functional changes.<sup>5-7</sup> Histopathological findings in selected cases demonstrate erythrocyte extravasation and capillary ectasia, supporting these mechanisms.<sup>5,6</sup>

Diagnosis is clinical, and routine laboratory and imaging investigations are usually normal.<sup>2-4</sup> The dramatic presentation often leads to suspicion of acute ischemia, vasculitis, Raynaud's phenomenon, digital venous thrombosis, or Gardner-Diamond syndrome, but these conditions differ in clinical evolution, systemic involvement, or laboratory abnormalities.<sup>2</sup> Recognition of the typical presentation can prevent unnecessary use of Doppler ultrasound, Computed Tomography angiography, echocardiography, or autoimmune testing.<sup>4</sup> No treatment is advised. Increased clinical recognition can reduce patient anxiety, limit unnecessary investigations, and prevent inappropriate referrals to specialties such as rheumatology, hematology, or vascular surgery.<sup>5-7</sup>



**Figure 1.** A and B: violaceous discoloration and mild swelling of the third left finger. C: nail bed and fingertip are spared.

## Conclusion

Achenbach syndrome is a benign, self-limited vascular condition that should be diagnosed clinically. Awareness of its characteristic presentation allows clinicians to avoid unnecessary investigations and provides reassurance to patients experiencing this alarming but harmless condition.

## Funding

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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.

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's

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### **Declaration on the use of artificial intelligence.**

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# Linear immunoglobulin A bullous dermatosis in childhood with an atypical granular pattern: importance of early differential diagnosis

*Dermatose bolhosa por IgA linear infantil com padrão granular atípico: importância do diagnóstico diferencial precoce*

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## Abstract

Linear immunoglobulin A bullous dermatosis (LABD) is a rare autoimmune blistering disease, more frequent in childhood, characterized by vesiculobullous lesions and linear immunoglobulin A (IgA) deposition along the basement membrane zone. We report the case of a 4-year-old child with typical LABD lesions but showing a granular IgA pattern on direct immunofluorescence, raising a diagnostic consideration of dermatitis herpetiformis. However, negative serologic tests and the absence of gastrointestinal symptoms, along with a favorable response to dapsone despite no gluten-free diet, supported the diagnosis of LABD. Bullous impetigo, bullous pemphigoid, and epidermolysis bullosa acquisita were excluded based on clinical and immunopathological features. This case underscores the importance of early clinical recognition and accurate differential diagnosis, even in the presence of atypical findings. Prompt initiation of dapsone led to complete remission, emphasizing the critical role of dermatologists in ensuring optimal outcomes in this uncommon condition.

**Keywords:** Linear immunoglobulin A bullous dermatosis. Dermatitis herpetiformis. Dapsone. Direct immunofluorescence.

## Resumo

A dermatose bolhosa por IgA linear (DBAL) é uma doença autoimune rara, mais frequente na infância, caracterizada por lesões vesicobolhosas e deposição linear de IgA na zona da membrana basal. Relatamos o caso de uma criança de 4 anos com lesões típicas de DBAL, mas com padrão granular de IgA à imunofluorescência direta, aventando a possibilidade diagnóstica de dermatite herpetiforme (DH). No entanto, a negatividade dos testes sorológicos e a ausência de sintomas gastrointestinais, associadas à resposta clínica favorável à dapsona, mesmo sem restrição dietética ao glúten, confirmaram o diagnóstico de DBAL. Impetigo bolhoso, penfigoide bolhoso e epidermólise bolhosa adquirida foram excluídos com base em critérios clínicos e imunopatológicos. Este caso destaca a importância do reconhecimento clínico precoce e do diagnóstico diferencial preciso, mesmo diante de achados atípicos. O início do tratamento com dapsona levou à remissão das lesões, reforçando o papel fundamental do dermatologista no manejo dessa condição rara.

**Palavras-chave:** Dermatose bolhosa por IgA linear. Dermite herpetiforme. Dapsona. Imunofluorescência direta.

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## Introduction

Linear immunoglobulin A bullous dermatosis (LABD) is a rare autoimmune subepidermal blistering disorder characterized by linear immunoglobulin (Ig)A deposition along the basement membrane zone (BMZ).<sup>1</sup> It affects both adults and children, being more frequent in the latter, typically between 4 and 5 years of age.<sup>2</sup> In pediatric cases, it is also termed chronic bullous disease of childhood.<sup>3</sup> Lesions are polymorphic, presenting as tense vesicles or bullae, urticarial plaques, or erythematous papules. Common sites include the perioral region, wrists, ankles, and thighs. In children, the lower abdomen and anogenital area are often affected, with vesicles arranged in annular or arciform patterns forming the characteristic “string of pearls” or “rosette-like” configurations.<sup>1,2</sup> Mucosal involvement, particularly in the conjunctiva and oral cavity, is also frequent.<sup>4</sup>

The main differential diagnoses are dermatitis herpetiformis (DH) and bullous pemphigoid (BP).<sup>5</sup> The hallmark of LABD is a linear IgA band on direct immunofluorescence (DIF), but atypical granular deposition may occur, complicating the distinction from DH.<sup>3</sup>

Given the rarity of the disease, its clinical overlap with other bullous dermatoses, and the importance of timely treatment, this case report emphasizes the crucial role of the dermatologist in establishing an accurate diagnosis, initiating appropriate therapy, and ensuring close follow-up to prevent adverse outcomes.

## Case report

A 4-year-old male was referred to the dermatology department for the sudden onset of intensely pruritic vesicles containing yellowish-citrine fluid. According to his parents, lesions had appeared 6 months earlier, initially in the perioral region, and rapidly disseminated across the body, evolving into erosions and crusts. Previous treatment with topical corticosteroids and oral cephalexin was ineffective. His parents denied systemic symptoms, and no close contacts had similar lesions.

On examination, he presented polymorphic lesions including vesicles, bullae, erosions, and crusts. Some vesicles were arranged circumferentially around a central ulcerated or necrotic area on an erythematous base, forming annular plaques with tense peripheral vesicles - the characteristic “string of pearls” or “rosette-like” pattern. Lesions were distributed on the lower and upper limbs and the cervical region (Figs. 1A-C). No mucosal involvement was observed.

Based on the characteristic appearance of the lesions, LABD was the leading clinical diagnosis. A skin biopsy, DIF, and laboratory tests before dapsone initiation – the treatment of choice – were requested. Histopathological analysis of perilesional skin from the left leg revealed epidermis with irregular acanthosis, mild spongiosis, and hyperparakeratosis, along with a fibrinoleukocytic crust. The superficial dermis showed a mild perivascular lymphocytic and neutrophilic infiltrate with congestion and edema. DIF demonstrated granular IgA deposits along the BMZ, while IgG, IgM, and C3 were negative (Figs. 2A and B). Salt-split skin testing and in indirect immunofluorescence (IIF) were unavailable. Complete blood count, renal and liver function tests, and glucose-6-phosphate dehydrogenase (G6PD) levels were normal.

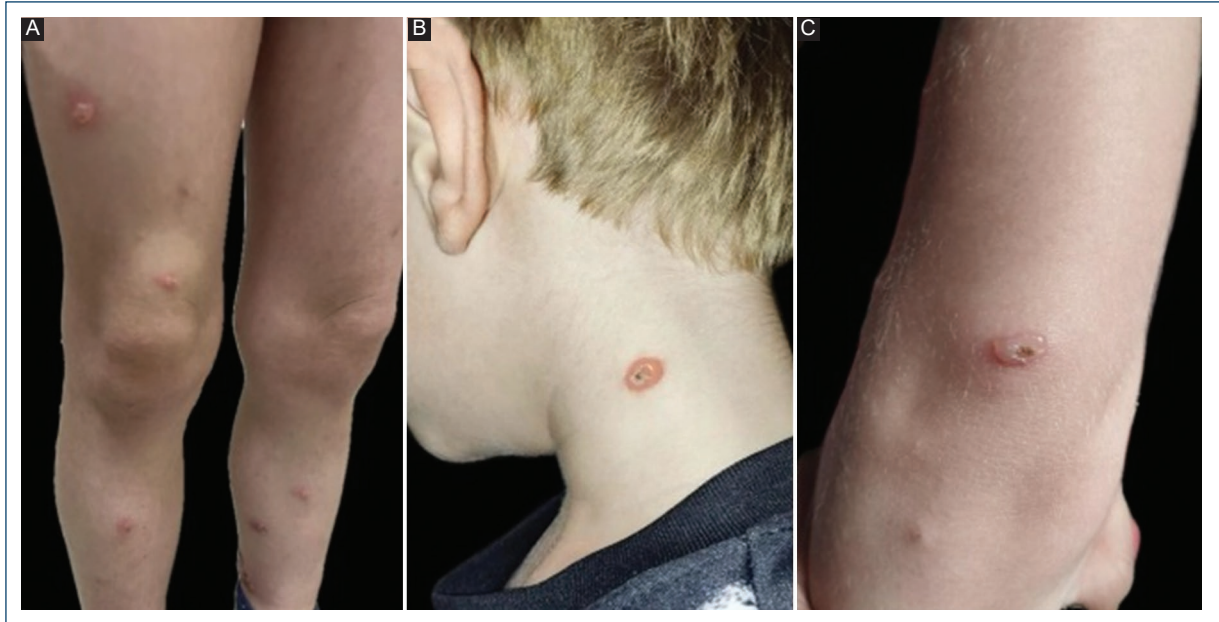
Due to the granular IgA pattern, the patient was referred to gastroenterology to investigate DH. Serologic testing was negative for anti-endomysial IgA and IgG antibodies and anti-tissue transglutaminase IgA antibodies. In addition, there were no gastrointestinal symptoms, namely on exposure to gluten, which further supported the exclusion of DH.

The differential diagnosis also included bullous impetigo, BP, and epidermolysis bullosa acquisita (EBA). The absence of clinical or laboratory evidence of bacterial infection, poor response to antibiotics, and the typical rosette-like arrangement of tense vesicles on seemingly healthy surrounding skin ruled out bullous impetigo. BP and EBA were considered unlikely given the patient’s age, lesion distribution, and negative IgG and C3 on DIF.

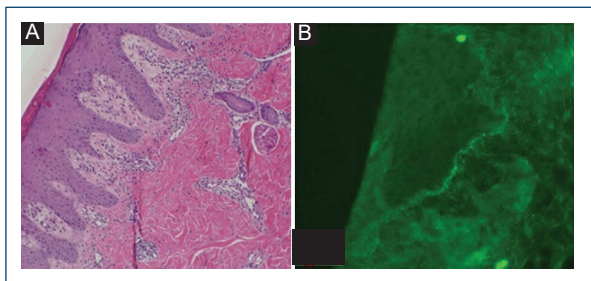
The case was therefore managed as LABD, based on the classic clinical presentation and exclusion of other differentials. Dapsone was initiated at a dose of 0.5 mg/kg/day, but lesions persisted at this dosage. Increasing the dose to 1 mg/kg/day led to full remission within 1 month, despite the absence of a gluten-free diet. The patient remains on maintenance therapy with dapsone 1 mg/kg/day and under quarterly clinical and laboratory follow-up, with no residual or recurrent lesions and no evidence of adverse effects or drug-related toxicity to date.

## Discussion

First described by Bowen in 1901,<sup>6</sup> LABD is the most frequent autoimmune blistering disease in childhood,<sup>4,7</sup> though it remains rare, with an estimated incidence of 0.5-2.3 cases per million individuals per year.<sup>4</sup> Blister formation results from an autoimmune response in



**Figure 1.** Clinical images. **A:** multiple tense and grouped vesicobullous lesions, presenting a “rosette-like” appearance on the lower limbs. **B:** in detail, lesions arranged in an annular confluence around a vesiconecrotic center on seemingly healthy skin, located in the cervical region. **C:** vesicobullous lesion with central ulceration, located on the upper limb.



**Figure 2.** Histopathology and direct immunofluorescence with granular IgA deposition. **A:** incisional biopsy of a skin lesion on the distal third of the left leg, consistent with a skin fragment showing epidermis with irregular acanthosis, mild spongiosis, and hyperparakeratosis, in addition to an area covered by a fibrinoleucocytic crust. The superficial portion of the dermis shows a mild inflammatory infiltrate composed of lymphocytes and neutrophils, along with congestion and edema. Hematoxylin-eosin,  $\times 10$ . **B:** direct immunofluorescence of skin from the distal third of the left leg demonstrating granular deposits of immunoglobulin A in the basement membrane zone. Direct immunofluorescence,  $\times 10$ .

which IgA-class autoantibodies target antigens in the BMZ of the skin and mucous membranes,<sup>1</sup> disrupting dermal-epidermal adhesion and leading to cleavage at multiple levels.<sup>5</sup>

The primary antigenic targets identified in LABD are the 97-kDa and 120-kDa fragments of BP antigen 2 (BP180/collagen XVII),<sup>1,2,4</sup> a transmembrane protein essential for dermal-epidermal adhesion, located in the lamina lucida.<sup>4</sup> Although most cases are idiopathic,<sup>1,2,4,7</sup> drug-induced LABD – particularly related to vancomycin – has been described in adults.<sup>1,4</sup> Genetic predisposition has been associated with HLA types HLA-B8, HLA-DR3, HLA-DQ2, and HLA-Cw7.<sup>2,4,7</sup>

Clinically, LABD may present with tense, scattered bullae on normal-appearing skin or herpetiform lesions on an erythematous base. Lesions may contain serous or hemorrhagic fluid. In children, the classic “string of pearls” pattern manifests as annular erythematous plaques with peripheral vesicles,<sup>2,4</sup> as observed in our patient. This rosette-like arrangement, caused by new vesicle formation at the edges of resolving lesions, is uncommon in adults.<sup>1</sup> Pediatric cases typically affect the lower abdomen, thighs, and groin, whereas adult forms more often involve the extensor surfaces, face, and trunk.<sup>1</sup> A short prodromal phase with intense pruritus or systemic symptoms such as fever and anorexia may precede the onset of lesions.<sup>5</sup>

With proper treatment, lesions usually resolve without scarring, although residual pigmentation may persist.<sup>5</sup> Mucosal involvement is also common, particularly

in the oral and ocular regions.<sup>1,4</sup> Oral lesions include painful ulcers, erosive or desquamative gingivitis, and occasionally, scarring.<sup>1</sup> Ocular involvement may cause conjunctival hyperemia, ocular discharge, pain, or foreign body sensation; chronic inflammation can result in synechiae or even vision loss.<sup>4</sup>

Due to its broad clinical spectrum, LABD can clinically mimic other bullous diseases,<sup>8</sup> especially DH, a gluten-sensitive dermatosis characterized by pruritic erythematous papules and granular IgA deposition along the BMZ.<sup>9</sup> Therefore, definitive diagnosis requires a skin biopsy for hematoxylin-eosin histopathology and DIF.<sup>5</sup>

Histologically, LABD features a subepidermal blister with a predominantly neutrophilic infiltrate in the papillary dermis,<sup>1</sup> though lymphocytes and eosinophils may also be present.<sup>2</sup> In DIF, linear IgA deposition along the BMZ is the hallmark finding. However, approximately 20% of patients may display granular deposits.<sup>10</sup> Concomitant linear C3 and, less frequently, IgG deposits may be observed, though IgG staining is usually weaker than IgA. When IgG and IgA deposits show similar intensity, distinguishing LABD from BP or other subepidermal autoimmune blistering diseases – such as EBA – becomes challenging.<sup>10</sup> In the present case, IgG and C3 deposits were absent.

If a granular IgA pattern is observed, DH should be excluded through negative serologic testing for anti-tissue transglutaminase and anti-endomysial IgA antibodies.<sup>3</sup> In uncertain cases, salt-split skin immunofluorescence showing linear IgA deposition on the epidermal side of the split supports LABD.<sup>3</sup>

Although bullous impetigo, BP, and EBA were initially considered, clinical and immunopathological findings ruled them out. The tense, symmetric, non-fragile vesicles and negative DIF for IgG and C3 were inconsistent with both BP and EBA, while the absence of infection and resistance to antibiotic therapy excluded bullous impetigo.

Spontaneous remission may occur in children within 2-4 years of disease onset,<sup>7</sup> pharmacological treatment is usually required. Delayed diagnosis increases the risk of complications, including secondary infection<sup>5</sup> or ocular sequelae. Dapsone, a sulfone with immunomodulatory properties, is the first-line treatment. It is typically started at doses above 0.5 mg/kg/day and titrated as needed.<sup>7</sup> Most of the patients improve within days; lack of response should prompt diagnosis reassessment. This rapid improvement aligns with recent multicenter data showing marked benefit within the 1<sup>st</sup> week of dapsone therapy.<sup>11</sup>

Due to the risk of dapsone-induced hemolysis,<sup>5</sup> evaluation of G6PD levels before treatment and regular monitoring of blood counts, bilirubin, lactic dehydrogenase, and aminotransferases are essential.<sup>4,7</sup> Cutaneous lesions usually heal without scarring, although mucosal fibrosis may lead to functional impairment.

In DH, by contrast, dapsone provides only symptomatic relief, and strict adherence to a gluten-free diet remains the disease-modifying treatment needed to achieve sustained remission.<sup>12</sup>

This case describes a patient with typical clinical features of LABD but an atypical granular IgA pattern on DIF, underscoring the importance of comprehensive diagnostic evaluation and exclusion of differentials to ensure optimal outcomes. Despite the non-classical DIF pattern, the presence of rosette-like lesions and negative DH serology supported the clinical diagnosis of LABD. Prompt initiation of dapsone led to complete remission of the lesions despite the absence of a gluten-free diet, highlighting the importance of early recognition and treatment to prevent complications, reduce morbidity, and minimize recurrence in this rare and underrecognized dermatologic condition.

## Conclusion

This case demonstrates that linear immunoglobulin A bullous dermatosis (LABD) may present with an atypical granular pattern on direct immunofluorescence, leading to diagnostic uncertainty. Careful clinicopathological correlation and systematic exclusion of differential diagnoses, particularly dermatitis herpetiformis, are essential for establishing the diagnosis. The complete remission achieved with dapsone, even in the absence of a gluten-free diet, reinforces that early recognition of the disease and timely treatment can favorably modify the clinical course, reducing morbidity and preventing complications in pediatric patients.

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None.

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# Vancomycin-induced drug rash with eosinophilia and systemic symptoms syndrome: a case report

## Síndrome de reação a medicamentos com eosinofilia e sintomas sistêmicos induzido por vancomicina: relato de caso

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### Abstract

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is an uncommon but potentially life-threatening cutaneous hypersensitivity reaction characterized by extensive mucocutaneous eruption, fever, hematologic abnormalities, including eosinophilia and/or atypical lymphocytosis, and extensive organ involvement. Here, we present a rare case of DRESS syndrome in a female patient with burn injuries, following vancomycin therapy for methicillin-resistant *Staphylococcus aureus* infection. According to the RegiSCAR diagnostic criteria, the case was classified as definite DRESS. Clinical resolution was achieved with the timely initiation of methylprednisolone and antihistamine therapy.

**Keywords:** Drug reaction with eosinophilia and systemic symptoms syndrome. DRESS. Drug hypersensitivity syndrome. RegiSCAR. Vancomycin.

### Resumo

A síndrome de reação a drogas com eosinofilia e sintomas sistêmicos (DRESS) é uma reação cutânea de hipersensibilidade rara, porém potencialmente fatal, caracterizada por uma erupção mucocutânea extensa, febre, anormalidades hematológicas, incluindo eosinofilia e/ou linfocitose atípica, e envolvimento extenso de órgãos. Neste artigo, apresentamos um caso raro de síndrome DRESS em uma paciente com queimaduras, após tratamento com vancomicina para infecção por *Staphylococcus aureus* resistente à metilicina (MRSA). De acordo com os critérios diagnósticos do RegiSCAR, o caso foi classificado como DRESS definitivo. A resolução clínica foi alcançada com a introdução oportuna de metilprednisolona e terapia com anti-histamínico.

**Palavras-chave:** Síndrome de reação a drogas com eosinofilia e sintomas sistêmicos. DRESS. Síndrome de hipersensibilidade a drogas. RegiSCAR. Vancomicina.

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## Introduction

Adverse drug reactions affecting the skin are common and present with a diverse pattern of expressions. Cutaneous hypersensitivity reactions range in severity, from mild reactions to severe cutaneous adverse reactions (SCARs).<sup>1</sup> To be included in SCAR, the following criteria are to be fulfilled: (1) severe (associated to a significant morbidity and mortality and usually leading to hospitalization); (2) non-predictable (idiosyncratic, and probably of immunological mechanism); and (3) most often induced by drugs.<sup>1</sup> DRESS is a distinct SCAR characterized by potentially life-threatening hypersensitivity reaction with extensive rash, fever, and internal organ involvement, including liver and kidney, occurring most commonly 2-6 weeks after initiation of a medication.<sup>2</sup> Here, we describe a case of DRESS syndrome caused by vancomycin.

## Case report

A 62-year-old female was admitted to a tertiary care hospital presenting with high-grade fever, a progressively worsening maculopapular rash, peripheral eosinophilia, and evidence of hepatic and renal dysfunction. On examination, the patient was alert and fully oriented. A diffuse blanching erythema with desquamation was noted over the face, back, and extremities (Figs. 1-3), while the oral mucosa remained unaffected. No lymphadenopathy was detected. The patient's medical history revealed prior hospitalization for burn management, during which she was treated with vancomycin (2 g/day) for a MRSA infection. She denied any concurrent medications or known drug allergies. Approximately 3 weeks after initiating vancomycin therapy, she developed the aforementioned symptoms.

Laboratory investigations conducted both before and following the onset of symptoms (Table 1) demonstrated hematological abnormalities, impaired liver function, and declining renal parameters. Serological tests for hepatitis A, B, C, and E viruses, as well as human immunodeficiency virus (HIV)-1 and HIV-2, were all negative. A diagnosis of drug reaction with eosinophilia and systemic symptoms (DRESS) was established based on hematological findings, hepatic and renal involvement, and exclusion of other etiologies.

According to the RegiSCAR diagnostic criteria, the case was classified as "definite DRESS" with a score of 6, considering the presence of fever, eosinophilia ( $> 1500/\mu\text{L}$ ), atypical lymphocytes, rash involving over 50% of the body surface with purpuric features and



**Figure 1.** Drug reaction with eosinophilia and systemic symptoms syndrome with marked facial exfoliative dermatitis and swelling.



**Figure 2.** Generalized exfoliative dermatitis in the context of drug reaction with eosinophilia and systemic symptoms, with a detail on the forearms.

infiltration, and multi-organ involvement. The Naranjo adverse drug reaction probability scale yielded a score of 8, indicating a "probable" association with vancomycin. The patient was managed promptly with systemic corticosteroids methylprednisolone 125 mg (approximately

**Table 1.** Laboratory parameters before and after the onset of vancomycin

Investigations	Before starting of vancomycin	At 3 weeks of vancomycin	After stopping vancomycin and 7 days of methylprednisolone
Hemoglobin (g %)	9.6	9.5	9.5
Total leucocyte count (n/mm <sup>3</sup> )	7800	14,000	10,000
Polymorphs (%)	55	53	53
Eosinophils (%)	1	26	14
Absolute eosinophils count (/mm <sup>3</sup> )	200	3800	1900
Atypical lymphocytes	Absent	Present	Present
Platelets (/mm <sup>3</sup> )	2.3 × 10 <sup>5</sup>	2.3 × 10 <sup>5</sup>	2.23 × 10 <sup>5</sup>
Urea (mg/dL)	18	20	20
Creatinine (mg/dL)	1	3	2
Serum bilirubin (mg/dL)	0.8	3	1.3
Alanine aminotransferase (U/L)	26	152	91
Aspartate aminotransferase (U/L)	28	378	218
Alkaline phosphatase (U/L)	58	188	86
Antinuclear antibody	Negative	Negative	Negative
Urine protein	Nil	Traces	Traces



**Figure 3.** Details of the hand involvement in the case of generalized exfoliative dermatitis in the context of drug reaction with eosinophilia and systemic symptoms from vancomycin.

1.25 mg/kg daily, body weight 98.3 kg) for 3 days. She was treated with tapering oral prednisolone for an additional 2 weeks and antihistamines, resulting in

significant clinical improvement and normalization of hematological, hepatic, and renal parameters (Table 1).

## Discussion

The term DRESS was first proposed by Bocquet et al. in 1996.<sup>2</sup> DRESS is a dermatological emergency with a reported mortality rate of approximately 10%.<sup>3</sup> Its incidence is estimated at 1 in 1,000 to 1 in 10,000 drug exposures.<sup>4</sup> The underlying pathophysiology remains incompletely defined but is thought to involve an immune-mediated mechanism, potentially influenced by viral reactivation.<sup>5</sup> Early in the disease course, reductions in circulating B lymphocytes and serum immunoglobulin levels have been observed.<sup>5</sup> Elevated inflammatory cytokines are commonly present, with interleukin-5 often peaking several days before the onset of eosinophilia.<sup>6</sup>

Diagnosis relies on both clinical features and laboratory data. Typical lab findings include eosinophilia or atypical lymphocytosis, elevated transaminases, increased creatinine, and pyuria, indicating possible hepatic and renal involvement.<sup>7</sup> Our patient presented with fever, rash, eosinophilia, and transaminitis. Cutaneous symptoms generally appear 2-8 weeks after initiating the causative drug and

may continue after its withdrawal.<sup>7</sup> In this case, the rash developed 3 weeks after starting antibiotic therapy.

In the European registry of SCARs to drugs and collection of biological samples (RegiSCAR) study, a definitive drug-related cause was identified in 88% of DRESS cases, whereas the cause remained uncertain in only 2%.<sup>8</sup> In our patient's case, DRESS syndrome likely developed as a result of vancomycin exposure. Vancomycin is responsible for approximately two-thirds of antibiotic-related DRESS cases.<sup>9</sup> According to a study using electronic health records, 74% of DRESS incidents were linked to antibiotics, with the majority caused by vancomycin, followed by beta-lactams.<sup>10</sup>

Because the clinical symptoms of DRESS can vary widely, a scoring system called the RegiSCAR Criteria was developed to assist with diagnosis.<sup>11</sup> According to this system, the patient received a total of seven points: one point for fever, two points for eosinophilia over 1500/uL, two points for skin involvement and biopsy indicating a drug reaction, two points for kidney and lung involvement, and negative results for antinuclear antibody, blood cultures, and hepatitis tests. The criteria are scored from 4 to 9, with scores of < 2 excluding the diagnosis of DRESS, 2-3 being possible, 4-5 probable, and score > 5 being definite. In our case, the patient's RegiSCAR score was 6.

The cornerstone of management for DRESS syndrome involves discontinuation of the offending agent alongside corticosteroid therapy. Given vancomycin's extended half-life, hemodialysis may be considered in severe, refractory cases, with a single session capable of removing up to 50% of plasma vancomycin concentrations.<sup>12</sup> Our patient exhibited marked clinical and biochemical improvement following corticosteroid administration. Consequently, the patient was discharged with outpatient follow-up arranged to monitor resolution and facilitate corticosteroid tapering.

## Conclusion

Diagnosing DRESS is difficult due to its variable symptoms, which can resemble many other conditions. This challenge is heightened because DRESS typically appears later than other drug reactions, usually 2-6 weeks after starting a medication, rather than 1-3 weeks. However, quickly identifying the syndrome and stopping the offending drug is crucial, as DRESS can be life-threatening but is often reversible. More research is needed to improve early diagnosis and develop

better treatment guidelines to reduce the illness and death associated with this condition.

## 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 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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## Complication following treatment with a microneedling technique for a female pattern hair loss: hair dye-induced tattoo-like pigmentation

*Complicação pós microagulhamento em alopecia de padrão feminino: pigmentação semelhante a tatuagem induzida por tinta de cabelo*

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### Abstract

Microinfusion of drugs into the skin (MMP<sup>®</sup>) is a Brazilian microneedling technique that employs professional tattoo devices for the delivery of pharmacological agents in conditions such as female pattern hair loss. We report an unexpected complication in a 44-year-old female patient who underwent hair dyeing 2 days after the procedure and subsequently developed linear pigmentation on the scalp resembling a tattoo. Trichoscopy revealed pigment deposition at the needle entry points, likely resulting from penetration of the hair dye. Although adverse effects of MMP<sup>®</sup> are generally mild, this case highlights the importance of counseling patients regarding the use of hair dye following the procedure.

**Keywords:** Androgenetic alopecia. MMP<sup>®</sup>. Female pattern hair loss.

### Resumo

MMP<sup>®</sup> (microinfusão de medicamentos na pele) é uma técnica brasileira de microagulhamento que utiliza equipamentos de tatuagem profissional para administração de fármacos em condições como a Alopecia de padrão feminino (FPHL). Relatamos complicação inesperada em paciente feminina de 44 anos que realizou tintura capilar dois dias após o procedimento, evoluindo com pigmentação linear semelhante a tatuagem no couro cabeludo. A tricoscopia evidenciou depósito pigmentário nos pontos de entrada das agulhas, provavelmente decorrente da penetração da tintura. Embora os efeitos adversos do MMP<sup>®</sup> sejam, em geral, leves, este caso reforça a necessidade de orientar pacientes quanto ao uso de tinta capilar após o procedimento.

**Palavras-chave:** Alopecia androgenética. MMP<sup>®</sup>. Alopecia de padrão feminino.

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## Introduction

MMP<sup>®</sup>, an acronym for microinfusion of drugs into the skin, is an innovative technique developed in Brazil that consists of microneedling performed with professional tattoo devices for the transdermal delivery of pharmacological agents.<sup>1</sup> It has been applied as an adjuvant treatment for androgenetic alopecia, particularly in cases of female pattern hair loss.<sup>2,3</sup> The method enables uniform infusion of substances into the dermis at an average depth of 1.0 to 1.5 mm, adjusted according to the clinical condition<sup>1</sup>. The procedure is generally well tolerated, with no reports of severe adverse events.<sup>3</sup>

This article describes the case of a patient who developed an unexpected complication following MMP<sup>®</sup> on the scalp, addressing its clinical, trichoscopic, and therapeutic aspects.

## Case report

A 44-year-old female patient underwent a session of MMP<sup>®</sup> on her scalp, utilizing minoxidil and dutasteride to treat FPHL (Fig. 1). Two days post-procedure, she dyed her hair and unexpectedly observed several linear scalp pigmentations, which caused her significant distress. In the following days, trichoscopic examination revealed pigmentation at the entry points of the microneedles from the MMP<sup>®</sup> procedure, resembling a tattoo, likely due to hair dye impregnation (Fig. 2). To address this issue, a daily regimen of exfoliating shampoo and a topical solution containing corticosteroids

and salicylic acid was recommended. Fortunately, after 7 days, the patient achieved complete resolution of the scalp pigmentation.

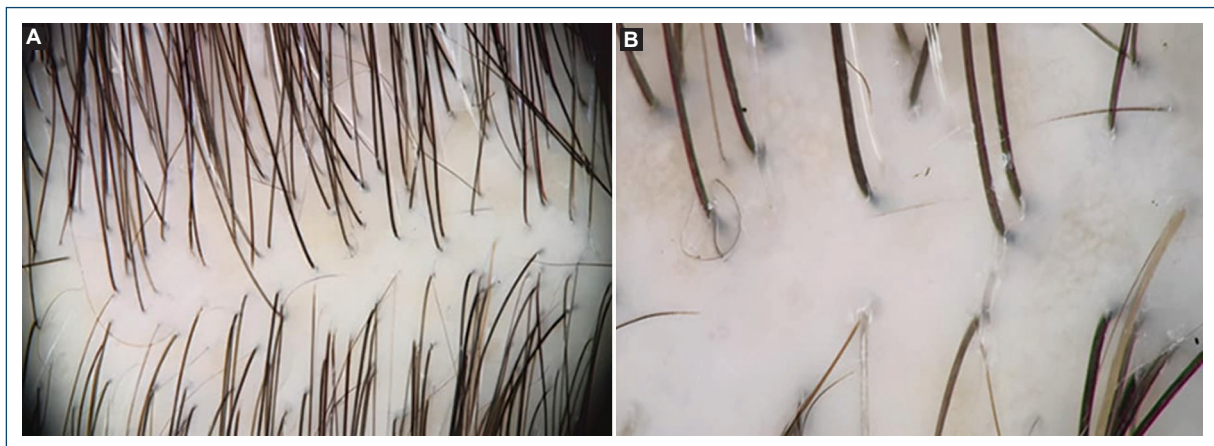
## Discussion

The MMP<sup>®</sup> procedure is performed using the Cheyenne tattoo machine along with sterile 27-Magnum needle cartridges to infuse medication into the skin.<sup>2</sup> The entry holes created by the 27-needle cartridge range from 6 to 10 microns in diameter, significantly smaller than the 0.3 mm diameter of a traditional needle shaft.<sup>1,2</sup>

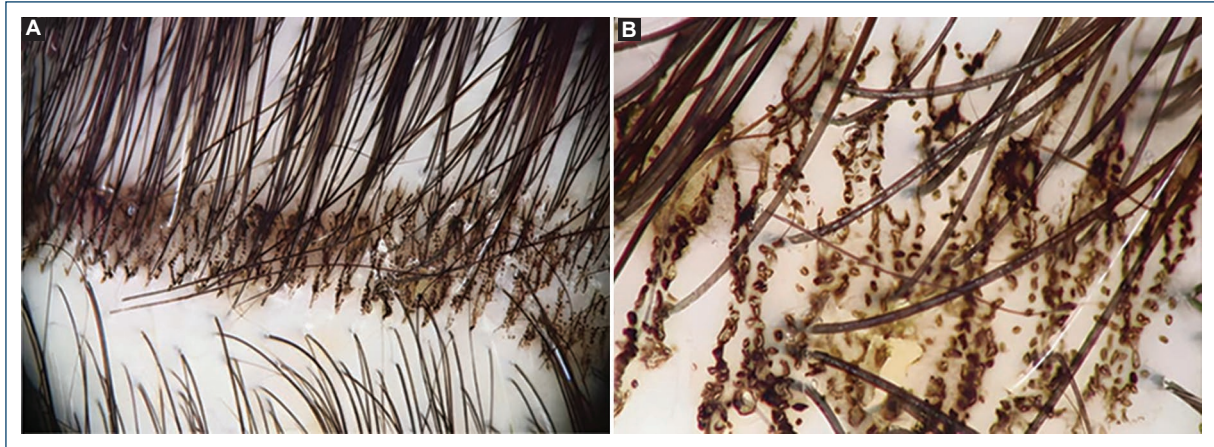
While previous reports have suggested that MMP<sup>®</sup> openings close within approximately 4 h, thereby limiting further drug permeation, our case challenges this notion.<sup>4</sup> The patient experienced temporary tattoo-like linear pigmentations resulting from topical particles applied 2 days after the MMP<sup>®</sup> procedure.

Overall, MMP<sup>®</sup> is associated with mild side effects, such as temporary pain and erythema at the application site, with no serious adverse events reported<sup>3</sup>. In this article, we present an additional side effect of MMP<sup>®</sup> that has not been previously described; nevertheless, it remains a safe treatment option.

This report underscores a potential post-procedure complication that can lead to both psychological and cosmetic concerns. It raises important questions regarding the optimal timing for recommending the use of hair dye, makeup, and hair fibers after MMP<sup>®</sup>,



**Figure 1.** Trichoscopy before the MMP<sup>®</sup> procedure. Magnification: **A:**  $\times 20$  and **B:**  $\times 70$ .



**Figure 2.** Trichoscopy after MMP<sup>®</sup> procedure. Images reveal the pigmentation at the entry points of the micro-needles. Magnification: **A:**  $\times 20$  and **B:**  $\times 70$ .

emphasizing the need to advise patients to observe a longer waiting period than previously believed before applying hair dye. Dermatologists must remain vigilant about this complication, particularly as MMP<sup>®</sup> gains popularity in treating common conditions like FPHL.

MMP<sup>®</sup> remains a safe option for the adjuvant treatment of Androgenetic Alopecia. Despite the report of another unexpected adverse event, its side effects are few, temporary, and not severe.

This article emphasizes the need for dermatologists to advise patients on delaying the use of hair dye and similar products after MMP<sup>®</sup> treatment to prevent cosmetic concerns. This report calls for increased awareness of potential complications as MMP<sup>®</sup> becomes more widely adopted for treating FPHL.

## Funding

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## Conflicts of interest

None.

## Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable 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 or creation of the content of this manuscript.

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## Apocrine hidrocystoma of the breast: a case report of unusual clinical and dermoscopic findings

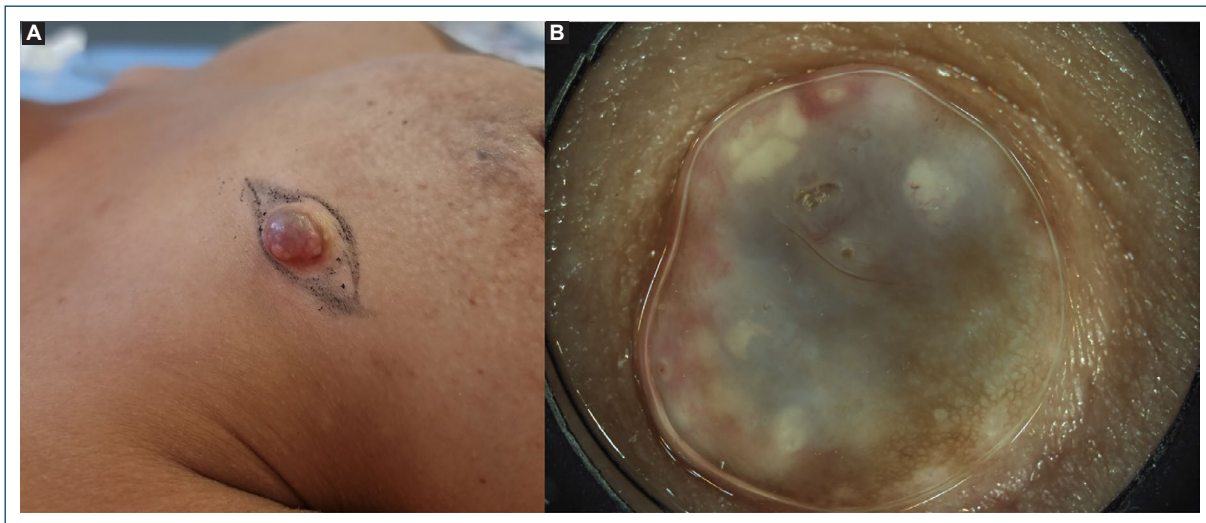
### *Hidrocistoma apócrino mamário: um caso com aspetos clínicos e dermatoscópicos invulgares*

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A 33-year-old woman presented with a 6-month history of a gradually increasing papule on her right breast. A 17 mm red-violet, asymptomatic, relatively indurated dome-shaped nodule was identified (Fig. 1A). Dermoscopic examination (Fig. 1B) revealed a central

homogeneous bluish-gray area with a few short linear-irregular vessels, an erythematous area with shiny whitish structures and a pigmented pseudo-network. Ultrasound examination revealed a cystic hypoechoic mass. Excision of the lesion was proposed, and the



**Figure 1.** Clinical images. **A:** clinical picture of the dome-shaped nodule on the right breast; **B:** dermoscopy of the apocrine hidrocystoma in vivo before excision.

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patient was at her 36th week (+4 days) of pregnancy on the day of the procedure. Histologic examination revealed an apocrine hidrocystoma.

Apocrine hidrocystomas are benign tumors of the apocrine sweat glands most frequently found on the head and neck.<sup>1</sup> Few have been reported in other areas.<sup>1-4</sup> Most grow to sizes varying from 1 to 10 mm; there are only few reports of larger lesions.<sup>2</sup> Our dermoscopic findings do not correspond to the most frequent patterns reported by Zaballos et al.<sup>1</sup> gray and pink homogenous areas and linear-irregular vessels were only found in 4.8% and 9.1% of reported cases; moreover, pigmented pseudo-networks have not been described.<sup>1</sup> In the differential diagnosis, atypical dermatofibroma, pigmented basal cell carcinoma, amelanotic melanoma or other adnexal tumors should be considered, particularly when atypical dermoscopic findings are present.<sup>3</sup> We hypothesize that a pigmented pseudo-network may have been caused by irritation derived from a chronic inflammatory process. The atypical findings of our hidrocystoma enhance the need for physicians to be aware of uncommon locations and dermoscopic findings of these lesions.

## Funding

None.

## Conflicts of interest

None.

## Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable 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 or creation of the content of this manuscript.

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# A case of primary cutaneous mucinous carcinoma in the scalp

## Um caso de carcinoma mucinoso primário cutâneo no couro cabeludo

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An otherwise healthy 80-year-old woman presented with a 2-year history of a progressively growing nodule on the scalp, without pain, bleeding, or discharge. The physical examination showed an erythematous-violaceous cupuliform nodule on the left occipital region, measuring 18 × 15 mm (Fig. 1A). No lymphadenopathy was noted. Histopathological examination revealed a circumscribed dermal nodule with pools of mucin separated by thin fibrous septa (Figs. 1B and C), containing islands of neoplastic epithelial cells with eosinophilic cytoplasm, small central nuclei, minimal pleomorphism and no mitotic activity (Fig. 1D), suggestive of primary cutaneous mucinous carcinoma (PCMC). The lesion was excised with clear margins. Extensive diagnostic workup, including breast and pelvic ultrasound, mammography, upper gastrointestinal endoscopy, colonoscopy, maxillofacial, cervical, thorax, abdomen, and pelvis computed tomography ruled out distant primary malignancy. No local recurrence, regional lymph node involvement, or distant metastasis was observed during 2-year follow-up. PCMC

is a rare neoplasm arising from eccrine glands and primarily affecting the head and neck area.<sup>1</sup> The difficulty of distinguishing this primary neoplasm from metastatic carcinoma of non-cutaneous origins (lung, breast, colon, others) presents a diagnostic challenge.<sup>1,2</sup> Microscopically, it is characterized by nests of neoplastic epithelial cells floating in mucinous lakes, with more organized nests, less hyperchromasia, and less mitosis compared to secondary mucinous metastasis. Immunohistochemical markers aid in the diagnosis, but still inconsistently differentiate PCMC from metastatic mucinous adenocarcinomas, so complementary evaluation, such as mammography, gastrointestinal endoscopy, computed tomography, and/or positron emission tomography, should be performed.<sup>2-5</sup> This case highlights histological features and diagnostic complexity of PCMC.

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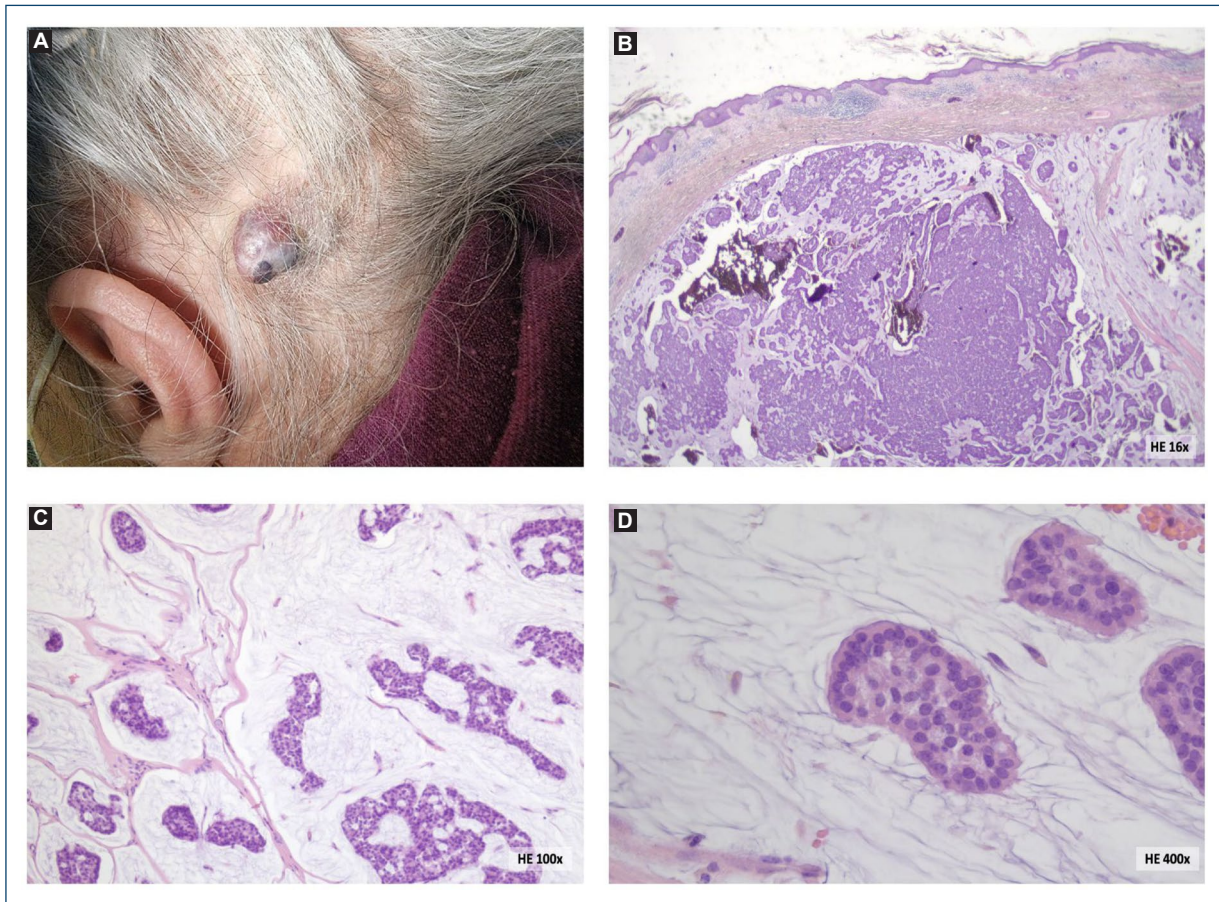
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**Figure 1.** Clinical images. **A:** elevated, dome-shaped, erythematous-violaceous nodule on the left occipital region; **B** and **C:** circumscribed dermal nodule with pools of basophilic mucin divided by thin fibrous septa creating a honeycomb pattern (more evident at right inferior edge); **D:** within the mucin lakes, “floating” islands of neoplastic epithelial cells with round to cuboidal shape, abundant eosinophilic cytoplasm, small central nuclei, minimal nuclear pleomorphism, and no mitotic figures.

## Conflicts of interest

None.

## Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution’s confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable 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 or creation of the content of this manuscript.

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## Erythematous lesions on the face of an 18-month-old girl

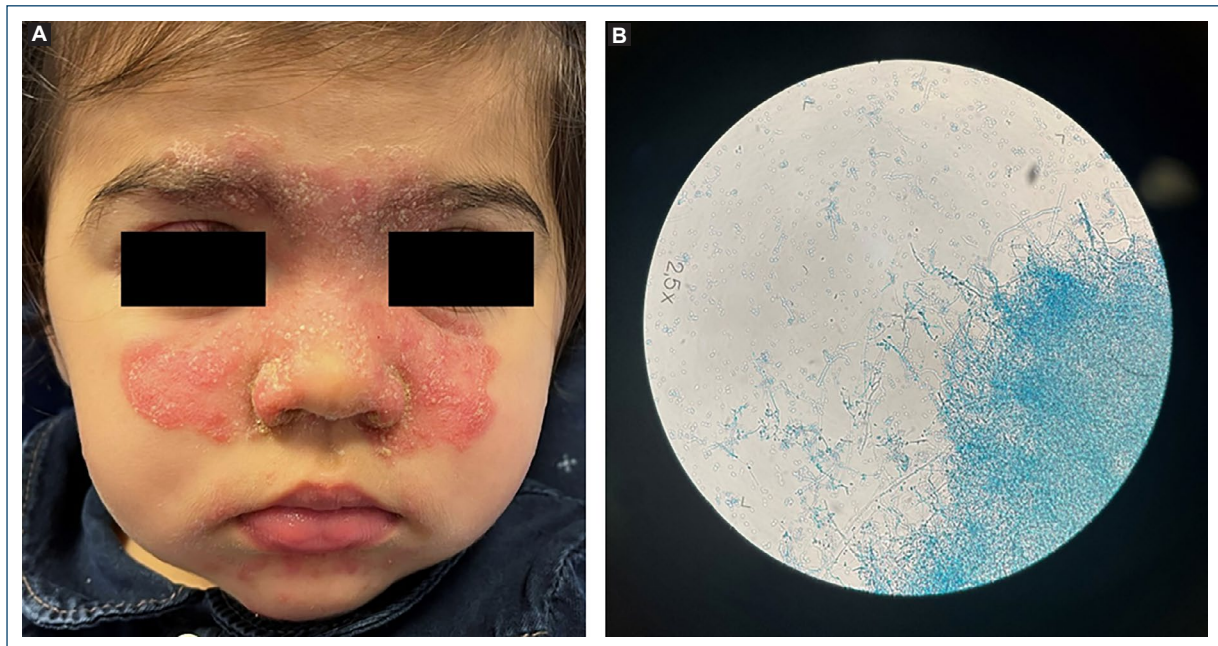
### Lesões eritematosas no rosto de uma menina de 18 meses

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An 18-month-old girl was evaluated for pruritic facial lesions evolving over 2 months. She was healthy, with no personal or family dermatological history. She frequently visited her grandmother's farm, where she had

contact with chickens and rabbits. Examination revealed a symmetrical, erythematous butterfly-shaped plaque occupying the central facial region, extending to the glabella and supraorbital areas, covered by yellowish



**Figure 1.** Clinical images. **A:** clinical findings showing erythematous butterfly-shaped plaque on the central facial region, covered by yellowish scales; **B:** microscopic examination of culture specimens identified clusters of microconidia and spiral hyphae, consistent with *Trichophyton mentagrophytes* (var. *granulosum*).

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scales (Fig. 1). The parents reported prior application of methylprednisolone aceponate cream, which worsened the dermatosis.

## What is the diagnosis?

### *Tinea incognita*

A mycological examination showed septate filaments on direct microscopy. Microscopic examination of culture specimens identified clusters of microconidia and spiral hyphae, consistent with *Trichophyton mentagrophytes* (var. *granulosum*). The diagnosis of *tinea incognita* (TI) was established.

TI is a dermatophytosis altered by topical corticosteroids or calcineurin inhibitors, masking its clinical features.<sup>1</sup> It commonly affects children aged 10-14 years and is rare in those under 3 years.<sup>2,3</sup> The face is frequently involved, as *tinea faciei* can be diagnostically challenging.<sup>2,3</sup> Hyphal invasion of hair follicles often necessitates oral antifungal treatment.

*T. mentagrophytes* var. *granulosum* is a zoophilic dermatophyte associated with rabbits and small rodents. The child's frequent contact with rabbits at her grandmother's farm likely facilitated fungal acquisition. The zoophilic nature of the variant explained the lesions' inflammatory and progressive features.

The child was treated with oral itraconazole (5 mg/kg/day) for 4 weeks, achieving complete resolution of the skin lesions.

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None.

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## Ethical considerations

**Protection of human subjects and animals.** The authors declare that no experiments on humans or animals were performed 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 or creation of the content of this manuscript.

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# An atypical presentation of hand-foot-mouth disease

## Uma apresentação atípica da doença mãos-pés-boca

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Hand-foot-mouth disease (HFMD) is an acute infectious disease caused by enteroviruses, characterized by enanthem and maculopapular and/or vesicular cutaneous rash affecting the hands, feet, and perioral and perineal regions.<sup>1</sup> Less commonly, atypical HFMD can occur with an exuberant widespread rash, increasingly associated with coxsackievirus A6.<sup>2-4</sup>

A healthy 11-month-old boy, with an epidemiological context of conjunctivitis at kindergarten, presented to the pediatric emergency department with a 3-day history of fever and 1-week history of enanthem and pruritic papulovesicular rash in perioral region, scalp, limbs, hands, and feet, with plaques and tense bullae on the thighs, extensor surfaces, and hands and feet, involving fingers (Figs. 1 A-C). Nasopharyngeal swab was positive for enterovirus/rhinovirus. Impetiginized viral rash and eczema herpeticum were considered and the patient started on antibiotic and antiviral medication.

The exuberance of the rash prompted a dermatology consultation. Considering the clinical presentation and laboratory findings, and after a typical skin biopsy (Fig. 2), the diagnosis of HFMD was made. The antibiotic and antiviral medication was discontinued, and the infant was discharged after 4 days. 2 weeks later, the skin lesions had resolved, but the child developed onychomadesis.

While enterovirus infections in infants can vary in severity, coxsackie A6 is often linked to characteristic lesions, including those on the hand and feet and onychomadesis,<sup>5</sup> suggesting this patient may have been infected by this serotype, although it was not possible to confirm it.

This atypical presentation that delayed diagnosis, highlighting the need for clinicians to be aware of exuberant unusual clinical presentations and potential serious complications of HFMD, even in pediatric patients.<sup>4</sup>

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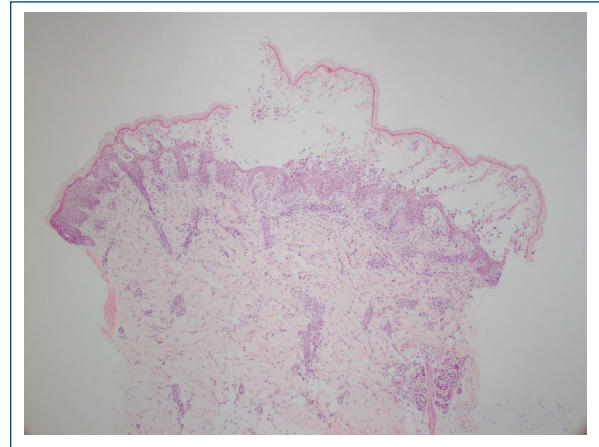
**Figure 1.** Clinical images. **A:** papulovesicular rash. **B:** hands and feet rash, involving the dorsum of feet and fingers. **C:** tense bubble in the extensor surface of the left arm.

### Funding

None.

### Conflicts of interest

None.



**Figure 2.** Skin biopsy, stained with hematoxylin-eosin, showed an intraepidermal vesicle with marked intracellular edema, focal superficial epidermal necrosis, with a mostly neutrophilic infiltrate, and a perivascular and interstitial mixed inflammatory infiltrate in the superficial dermis

### Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

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## Clinicopathological and imaging correlation of a cutaneous metastasis from renal cell carcinoma

### *Correlação clinicopatológica e imagiológica de uma metástase cutânea de carcinoma de células renais*

Hugo J. Leme<sup>1\*</sup>, José Ramos<sup>1</sup>, António Magarreiro-Silva<sup>1</sup>, Mário Amaro<sup>2</sup>, Ana I. Gouveia<sup>1</sup>, and João Alves<sup>1</sup>

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Dear Editor,

A 60-year-old woman with a prior right radical nephrectomy for clear cell renal carcinoma was admitted 18 months later with a 5-day history of expressive aphasia and right-sided motor weakness. During hospitalization, dermatology evaluated a 1.5 cm erythematous-violaceous nodule on the right flank, soft in consistency, evolving over several months (Fig. 1). Excisional biopsy revealed a dermal-based nodule with central necrosis and epithelioid cells with moderate atypia (Fig. 2). Immunohistochemistry was positive for CK AE1/AE3 and vimentin, consistent with cutaneous metastasis of renal origin. Concurrent staging with computed tomography and positron emission tomography (PET) identified a left frontal infra-axial lesion suggestive of brain metastasis, pulmonary nodules likely secondary, and probable peritoneal involvement. PET imaging demonstrated radiological-clinical correlation with the cutaneous lesion (Fig. 3).

Surgical excision confirmed brain metastasis from renal cell carcinoma. She received radiotherapy to the surgical bed and palliative sunitinib but died 5 months after starting treatment.



**Figure 1.** Erythematous-violaceous nodule on the right flank.

Cutaneous metastases from renal cell carcinoma are a manifestation of advanced disease, typically associated with poor prognosis, and may represent the first sign of metastatic spread.<sup>1</sup> Clinically, they show varied presentations and may mimic various benign and

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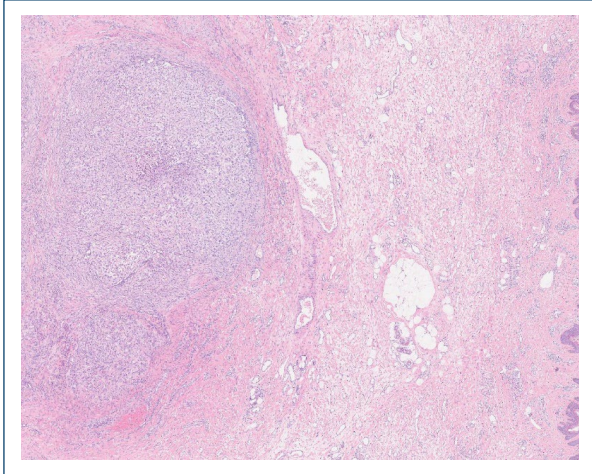
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**Figure 2.** Histology showing a dermal-based nodule with extensive central necrosis and epithelioid cells exhibiting moderate atypia (H&E x2).

malignant lesions, including hemangioma, pyogenic granuloma, angiosarcoma, and Kaposi sarcoma.<sup>1,2</sup> Surgical excision is the preferred treatment for solitary lesions.<sup>3</sup> However, up to 90% of cases occur with visceral metastases, explaining the poor prognosis and median survival under 6 months.<sup>3</sup>

As observed in this case, the cutaneous nodule preceded cerebral metastasis, and earlier detection might have influenced both prognosis and therapeutic approach.

### Funding

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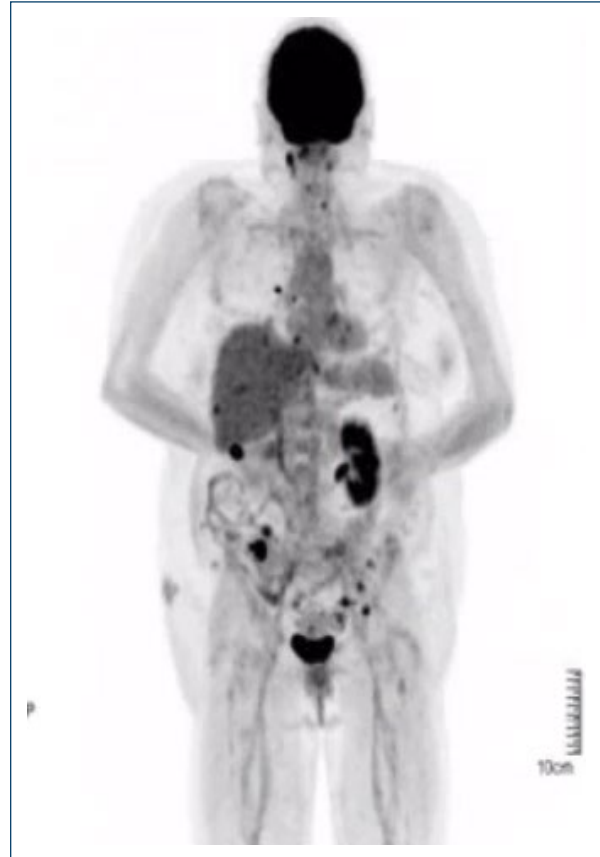
### Conflicts of interest

None.

### Ethical considerations

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

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's



**Figure 3.** PET scan showing a hypermetabolic lesion in the right flank (circled), corresponding to a confirmed metastasis. PET: positron emission tomography.

confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable 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 or creation of the content of this manuscript.

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## Assessment of TikTok content on hidradenitis suppurativa: a qualitative and quantitative analysis

### *Avaliação do conteúdo do TikTok sobre hidradenite supurativa: uma análise qualitativa e quantitativa*

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Dear Editor,

Hidradenitis suppurativa (HS) is a chronic, inflammatory dermatosis with profound psychosocial impact, often accompanied by pain, stigma, and depression.<sup>1,2</sup> The dissemination of health information through social media has expanded public access to medical knowledge, but the rapid and unfiltered spread of content also raises concerns regarding misinformation. TikTok, one of the fastest-growing social media platforms globally, has emerged as an important source of health-related information for younger audiences.<sup>3-5</sup> Given the vulnerability of patients seeking guidance online, a critical evaluation of HS-related content on TikTok is warranted. Motivated by this need, we conducted a qualitative and quantitative analysis of the most widely viewed TikTok videos related to HS to assess both content accuracy and audience engagement.

We performed a cross-sectional observational study in May 2025, using the search terms “hidradenite,” “hidradenite supurativa,” “hidradenitis,” and “hidradenitis suppurativa.” For each term, the 20 most-liked videos were collected, minimizing algorithm-driven selection bias. After removal of duplicates and irrelevant videos, 42 unique clips were included for analysis. Two independent reviewers assessed engagement metrics, content accuracy, and creator profile. Accuracy was evaluated through a pre-defined checklist addressing etiology,

diagnosis, and treatment. Engagement was calculated by summing likes, comments, saves, and shares divided by the creator’s total follower count.

The 42 selected videos amassed 3.77 million likes, 56,196 comments, and 338,775 shares. Most videos were in English (69.0%) and were produced predominantly by patients or influencers (40.5%). Dermatologists accounted for 23.8% of the content. Two main narrative styles emerged: personal accounts (n = 23) and educational explanations (n = 20). While most videos conveyed at least some accurate information (90.5%), key topics were frequently omitted. Only 11.9% specified that HS is not contagious, 7.1% mentioned known triggers, such as obesity and smoking, and just 2.4% disputed the myth that HS is related to poor hygiene.

A striking finding was the “engagement paradox”: low-credibility sources – those containing no correct information according to our predefined criteria – achieved disproportionately higher engagement (418.04%) compared with dermatologists (7.88%), despite the latter demonstrating 100% accuracy. This suggests that accuracy alone does not predict reach on TikTok and that emotionally charged or sensationalized content may be preferentially amplified.

TikTok’s expansion to over two billion monthly active users worldwide, with nearly 80% of its audience aged 18-34, underscores its influence as an emerging

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health-information ecosystem.<sup>6</sup> Brazil ranks among the countries with the highest number of users, and an estimated 40% of young adults now report preferring TikTok over Google for information searches.<sup>6</sup> Although our analysis demonstrates that accurate content is present on the platform, its visibility remains limited when compared with low-accuracy posts. The predominance of high-engagement misinformation highlights a potentially harmful dynamic: the platform's algorithm may inadvertently magnify misleading content, particularly which is emotionally salient, while suppressing medically reliable information.

Our findings align with prior research showing that misinformation about HS circulates widely on social networks, contributing to diagnostic delays, patient confusion, and stigma.<sup>4,5</sup> Importantly, the presence of correct but incomplete information may also reinforce misconceptions, such as the false association with hygiene or the neglect of modifiable risk factors. While social media offers unique opportunities to increase awareness of under-recognized diseases and shorten diagnostic timelines,<sup>7</sup> its unchecked influence demands active participation from healthcare professionals.

This study has limitations, including its cross-sectional design and relatively small sample size. TikTok's dynamic nature also means that trending content may shift rapidly, and engagement metrics can evolve over time. Nevertheless, the results provide a valuable snapshot of current HS-related discourse on one of the world's most influential platforms.

In conclusion, although most TikTok videos on HS contain at least partially correct information, significant knowledge gaps and high-engagement misinformation persist. Dermatologists and scientific societies should consider adopting proactive digital strategies, producing visually appealing and accessible content, and collaborating with credible influencers to expand the reach of evidence-based messages. Strengthening HS education on social media is essential to improving patient

outcomes, reducing stigma, and promoting accurate public understanding.

## Funding

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## Ethical considerations

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