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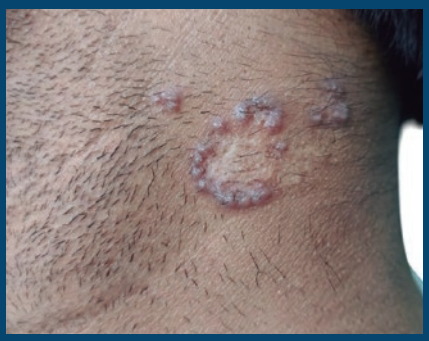

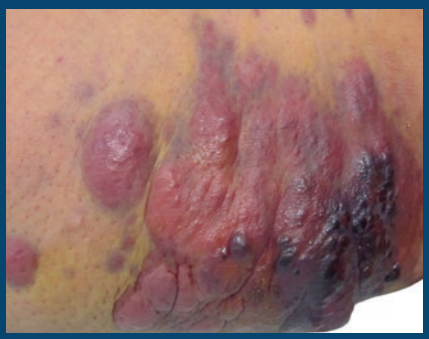

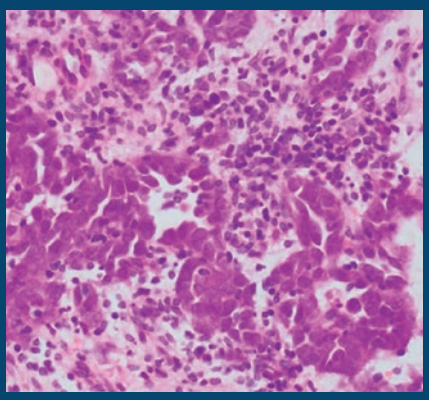

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REVIEW ARTICLE

Primary prevention strategies for melanoma

Estratégias de prevenção primária do melanoma

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Abstract

Melanoma is one of the malignancies whose frequency has increased with highest rate worldwide and accounts for most skin cancer-related deaths despite representing < 5% of cases. This review aimed to critically evaluate evidence on primary prevention strategies, their effectiveness, limitations, and outline priorities to reduce melanoma incidence. A systematic review was conducted in PubMed, MEDLINE, and Cochrane between November 2024 and January 2025. Eligible studies included adults (≥ 18 years), addressed primary prevention of melanoma, and were published since the year 2000. Thirty-five studies met inclusion criteria and were grouped into four themes: behavioral counseling and education (BC), technology-based interventions (T), genetic/personalized risk information (G), and chemopreventive agents (AQ). Daily sunscreen use emerged as a safe, effective, and cost-efficient measure. Protective clothing and shade-seeking complemented photoprotection but required combined use. Educational campaigns improved awareness and sun-protective behaviors, though impact varied with cultural adaptation and prevailing attitudes toward tanning. Technology-based strategies, including apps and short message service (SMS) reminders, showed potential in younger populations but limited long-term adherence. Genetic risk communication influenced preventive behaviors mainly in high-risk groups, with inconsistent effects in average-risk populations. Chemopreventive approaches, such as aspirin and long-chain n-3 polyunsaturated fatty acids, yielded conflicting results and remain inconclusive. Effective melanoma prevention requires a multifaceted approach integrating proven photoprotection, culturally tailored education, and innovative technologies. Sunscreen remains the cornerstone, but strategies must address tanning norms and population-specific needs. Future studies should emphasize long-term follow-up and cost-effectiveness in diverse populations.

Keywords: Melanoma. Primary prevention. Ultraviolet radiation. Sunscreen. Health education.

Resumo

O melanoma é uma das neoplasias malignas cuja frequência mais rapidamente tem crescido e é responsável pela maioria das mortes por cancro da pele, apesar de representar menos de 5% dos casos. Esta revisão teve como objetivo avaliar criticamente a evidência sobre estratégias de prevenção primária, a sua eficácia e limitações, e definir prioridades para reduzir a incidência do melanoma. Foi realizada uma revisão sistemática nas bases de dados PubMed, MEDLINE e Cochrane entre novembro de 2024 e janeiro de 2025. Foram incluídos estudos com adultos (≥ 18 anos), que abordassem a prevenção primária do melanoma, publicados a partir do ano 2000. Trinta e cinco estudos preencheram os critérios de inclusão e foram agrupados em quatro temas: aconselhamento comportamental e educação (AC), intervenções baseadas em tecnologia (T), informação genética/personalizada sobre risco (G) e agentes quimiopreventivos (AQ). A utilização diária de protetor solar

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surgiu como uma medida segura, eficaz e custo-efetiva. O vestuário protetor e a procura de sombra complementaram a fotoproteção, nomeadamente em combinação com outras estratégias de prevenção primária. As campanhas educativas melhoraram a consciência e os comportamentos de proteção solar, embora o impacto variasse consoante a adaptação cultural e as atitudes comportamentais face ao bronzeamento. Estratégias tecnológicas, como aplicações móveis e mensagens SMS, mostraram potencial em populações jovens, mas apresentaram baixa adesão a longo prazo. A comunicação de risco genético influenciou sobretudo grupos de alto risco, enquanto os resultados foram inconsistentes em populações de risco médio. Abordagens quimiopreventivas, como aspirina e ácidos gordos n-3 de cadeia longa, apresentaram resultados contraditórios e permanecem inconclusivas. A prevenção eficaz do melanoma requer uma abordagem multifacetada com integração de estratégias de fotoproteção, educação culturalmente adaptada e tecnologias inovadoras. Apesar da utilização de protetor solar mostrar-se como sendo a estratégia com maior custo-efetividade, poderá ser relevante a abordagem das normas sociais associadas ao bronzeamento e necessidades específicas da população. Estudos futuros devem priorizar o seguimento a longo prazo e a avaliação da custo-efetividade em diferentes contextos populacionais.

Palavras-chave: Melanoma. Prevenção primária. Radiação ultravioleta. Protetor solar. Educação em saúde.

Introduction

Melanoma is one of the types of malignant neoplasms that present the fastest growing incidence rate. Despite representings < 5% of all malignant skin neoplasms, it is globally responsible for the majority of deaths due to skin cancer[1].

In 2022, the occurrence of 331,000 cases of melanoma and about 57,000 deaths worldwide was estimated[2]. The highest incidence rates per 100,000 inhabitants were observed in Australia and New Zealand (42 in men and 31 in women), in Western Europe (19 in men and in women), in North America (18 in men and 14 in women), and in Northern Europe (17 in men and 18 in women)[3].

Incidence has been increasing over the past 50 years. In the United States, the probability of being diagnosed with invasive cutaneous melanoma increased from 1 in 1,500 in 1930 to 1 in 34 in 2015[4]. Estimates further indicate that 500,000 new cases of melanoma per year and 100,000 deaths are expected by 2040. This increase in incidence highlights the urgency of implementing specific and effective measures for melanoma prevention[3].

The main risk factors associated with melanoma are exposure to ultraviolet (UV) radiation, a history of sunburns (particularly in childhood), skin phototype (fair skin, red or blond hair, blue eyes), and personal or family history of melanoma. However, exposure to UV radiation, from sunlight or artificial sources, is described as the main environmental risk factor, associated with about 70% of cutaneous melanoma cases[5].

Melanoma is considered a highly preventable type of cancer. Primary and secondary prevention strategies can reduce incidence and potentially lower mortality. Primary prevention mainly consists of avoiding risk factors and adopting effective sun protection habits, while secondary prevention consists of early detection.

Avoiding both sun exposure and artificial tanning, and using protective clothing are also recommended photoprotection strategies, associated with a decreased risk of developing the disease.

The use of sunscreen is described as one of the fundamental strategies in primary prevention. It is estimated that it can reduce its incidence and the occurrence of invasive melanomas[6] and that its daily use is cost-effective and should be a priority in prevention[7].

Educational campaigns also play a fundamental role in raising public awareness about the risks of sun exposure and are tools for promoting effective sun protection behaviors and habits. However, it is important that these are adapted to the population's knowledge and beliefs so that motivation increases and leads to improvements in preventive behaviors.

Several studies also assess how technology, personalized risk assessment tools, and interventions tailored to risk profile can influence behavior change and, consequently, reduce or not the incidence of melanoma.

Although primary prevention strategies are today considerably recommended and studies support their effectiveness in melanoma prevention, historically some inconsistencies regarding their effectiveness[8] have been found[9]. For example, evidence regarding sunscreen use was quite inconsistent, although today it is considered an effective, safe[6], and cost-effective[10] measure.

Particularly at the level of primary health care, there is evidence regarding the effectiveness of behavioral counseling, population education, and awareness campaigns. However, there is still discussion about which theoretical approaches are most appropriate, what the ideal intensity and duration of counseling should be, and regarding appearance-based interventions (ABi)

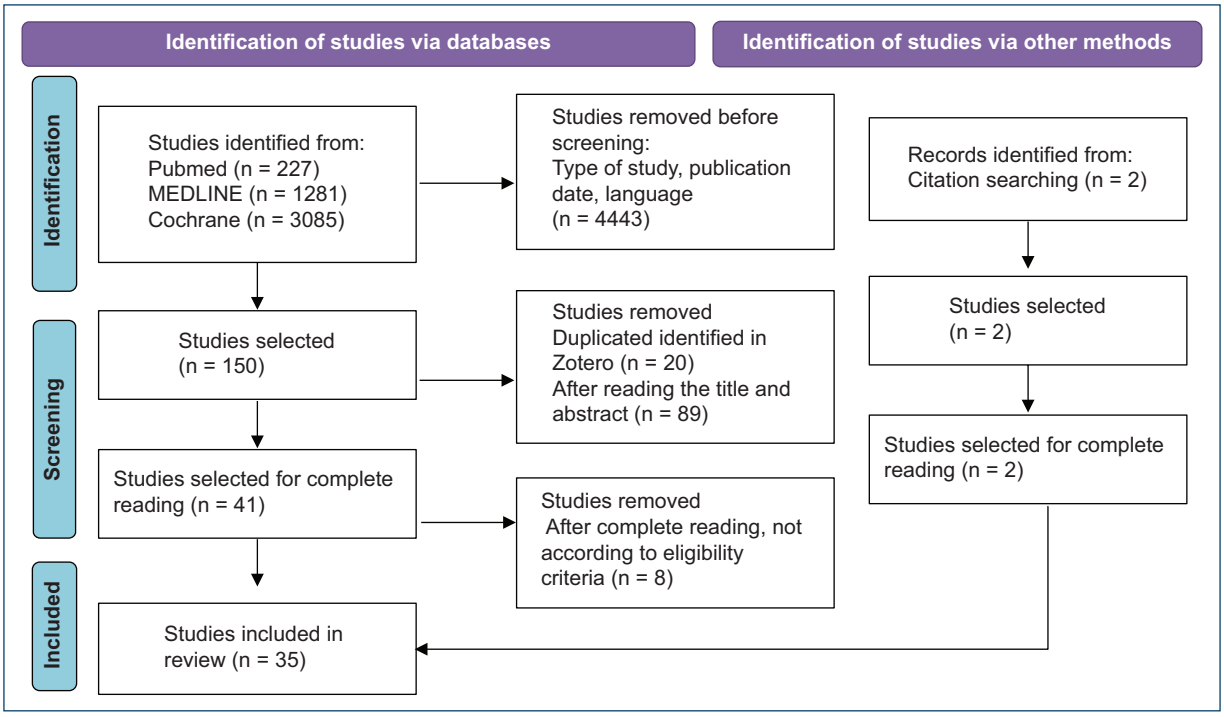

Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses flow diagram *(adapted from Page MJ, et al. BMJ 2021;372:n71.doi: 10.1136/bmj.n71)*[13].

(photoaging) compared to health-based interventions (HBi)[11].

Prevention measures involving genetic risk assessment and the provision of personalized information according to individual risk are also controversial. While several studies report that personalized interventions are more effective than generic ones, others do not appear to find greater effectiveness[12].

The effectiveness of using technology, such as digital interventions, mobile applications, and direct-to-consumer genetic testing in primary prevention, is also questionable[9]. Although technology is very promising in melanoma prevention, evidence on benefits and cost-effectiveness is still limited.

Thus, this work aims, through a literature review, to gather information about primary prevention strategies for melanoma, through an analysis of the most recent findings, inconsistencies, and limitations of 21st-century literature. It, therefore, seeks a better understanding of the effectiveness of different strategies, to identify priorities for future studies, and ultimately to optimize prevention strategies to reduce the incidence of melanoma.

Methodology

This study was conducted as a systematic review of the literature in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. The diagram in figure 1[13] presents the article selection process.

Search strategy and eligibility criteria

The PICO method was used to define the sample and the inclusion and exclusion criteria of the articles, which are presented in table 1.

P. Participants: adults aged 18 years or older.

I. Intervention: primary prevention strategies.

C. Comparison: other primary prevention strategies, no prevention strategy, secondary prevention strategies.

O. Outcome: incidence of melanoma/melanoma mortality/effectiveness of the applied strategy/frequency of sunburns/photoprotection behaviors.

A comprehensive literature search was performed in the following databases: PubMed, MEDLINE, and the Cochrane Library. The search was conducted between

Table 1. Eligibility criteria

Inclusion criteria	Population aged 18 years or older Inclusion of primary prevention strategies Publications from January 2000 to November 30, 2025 Articles in English, Portuguese, or Spanish Inclusion of melanoma Free articles or articles accessible through the Faculty of Medicine of the University of Lisbon
Exclusion criteria	Population under 18 years of age No inclusion of primary prevention strategies Publications before the year 2000 Articles in languages not included in the inclusion criteria (Portuguese, English, or Spanish) Exclusion of melanoma Paid articles or articles not accessible through the Faculty of Medicine of the University of Lisbon

November 2024 and January 2025. The search strategy was developed iteratively and combined controlled vocabulary terms and free-text keywords related to melanoma and primary prevention. Core search terms were combined using Boolean operators and the final search strategy was adapted for each database. The search carried out with Boolean operators through a single line approach, improved multiple times over time. The first search in November 2024 yielded 227 results in PubMed, 1,281 in MEDLINE, and 3,085 in Cochrane (Supplementary Table 1).

At the end of January 2025, after the different tests of the search strategy and changes in keywords, the results were limited to a total of 150 (54 results in PubMed, 10 in MEDLINE, and 86 in Cochrane) shown above. All the 150 articles were added to an Excel table reproduced in supplementary table 3, titles and abstracts of all articles were read, with identification of inclusion or exclusion criteria for eligibility.

Of the 150 articles, 61 were selected after screening of title and abstract ("eligibile" on Supplementary Table 3). The 61 articles were then added to the reference manager Zotero and, using this software, 20 duplicates were removed. After this, the 41 articles left were read in full. Of these 41 articles, 33 were selected as they fully met the eligibility criteria. An additional two articles were later found based on citation reading and included. In total, 35 articles were included in the systematic review.

The complete search strategy and procedure for all databases are detailed in the supplementary data.

Risk of bias assessment

Studies were evaluated for inclusion based on the predefined eligibility criteria. Each study was reviewed and decisions regarding inclusion were made based on these criteria. No independent formal risk-of-bias assessment was conducted.

Results

At the end 35 articles were included in the systematic review, with information regarding study type, participants, intervention and comparison, results, conclusions, limitations, and topic/primary prevention strategy presented in supplementary data.

The general themes/primary prevention strategies were divided into the following thematic codes:

- BC: behavioral counseling, education, and population awareness
- T: technology, mobile applications, online interventions, multimedia resources, and/or message sending
- G: genetic information, personalized risk information
- CQ: chemoprotective agents.

Discussion

From the studies included, eight focus on strategies of behavioral counseling, education, and population awareness (BC). Fourteen combined these approaches with the use of technology, online interventions, mobile applications, and/or message sending (T). Ten studies integrated behavioral counseling with the use of genetic information or personalized information on the individual risk (G). Three studies addressed the use of chemoprotective agents (CQ).

Behavioral counseling, education, and population awareness (BC)

Among primary melanoma prevention strategies, measures such as the use of sunscreen, protective clothing, seeking shade, and avoiding sun exposure during peak hours stand out across studies.

The use of sunscreen is consistently highlighted as an effective and accessible measure. Green et al. demonstrated that the regular use of sunscreen with a sun protection factor equal to or > 15 could be associated with up to a 73% reduction in the risk of developing invasive melanoma, and suggests that melanoma is, to a large extent, preventable through the regular use of sunscreen[6].

Hirst et al. and Gordon et al. concluded that the systematic use of sunscreen could prevent a significant number of new skin cancer cases and substantially contribute to the reduction of health care costs over up

to 30 years. Therefore, primary prevention based on the daily use of sunscreen was considered a strategic priority for investment in public health and considered superior to early detection at the population level[7,10].

On the other side, the early detection strategy seems to identify a greater number of melanomas at an early stage but also leads to the detection and treatment of a much larger number of benign lesions, resulting in higher costs and a slight negative impact on quality of life compared with the absence of intervention in some scenarios. Thus, the higher proportion of melanomas detected may not offset the risk of overdiagnosis and unnecessary treatments, economic burdens, and the slight negative impact on quality of life[7].

Regarding protective clothing, Yusufov et al. states that it is one of the most validated methods of photoprotection and that, together with the use of sunscreen, it may be more effective in preventing and reducing sunburns than the use of sunscreen alone[14].

Navarro-Bielsa et al. concluded that clothing was the least commonly used measure in their population (always or habitually, 22.8%). The melanoma group used clothing the least (13.7%) followed by the BCC group (22.2%), control group (26%), and SCC group (28.8%)[15].

The importance of combining different forms of photoprotection is highlighted, and it seems that none of these strategies should be viewed in isolation, but rather as part of an integrated set of preventive measures[16].

Several studies focus on the impact that educational and awareness interventions have on sun protection behaviors with the aim of reducing the risk of skin cancer or improving early detection. Many of these approaches make use of educational materials in print (such as leaflets) or digital (such as websites or short message service [SMS] messages), often including counseling – carried out by telephone, in person (by health professionals or genetic counselors), or integrated into structured programs.

Durand et al. suggest that ABi could be more effective in reducing sun exposure and improving sun protection, especially in groups with lower education levels and young adults. Emmons et al. also found a significant increase in the use of hats and sunscreen in the group that received biometric feedback, that is, the intervention group that viewed skin damage caused by exposure to UV radiation[17].

On the other hand, other studies in the literature cited by Durand et al. show mixed results in the comparison between ABi and HBi: some report greater effect of ABi, others no difference, or even a greater effect of HBi. This underlines the need for further research on which approaches work best for different populations and behaviors[11].

Byrne et al. highlights that, even in a group with high knowledge (medical students), positive attitudes toward tanning are associated with risk behaviors. High knowledge did not automatically translate into safe behaviors, and in fact, could be positively correlated with risk behaviors. This supports the idea that campaigns should focus more on changing attitudes and social norms (especially regarding tanning) rather than only on increasing knowledge[17]. Durand et al. incorporates the change in social norms regarding tanning into their ABi intervention, which may explain part of its effectiveness in reducing sun exposure. Aleo et al. also found low levels of knowledge in Italy, but behavioral outcomes were moderate/sufficient, suggesting that the knowledge–behavior relationship is complex and influenced by other factors such as attitudes and risk perception[11].

Regarding tanning, Byrne et al. identified positive attitudes toward tanning as a key driver of risk behaviors. Durand et al. states that tourists seek the sun and are particularly sensitive to the positive image of tanning, suggesting why ABi may be effective by highlighting the negative image of photoaging. Therefore, the persistence of positive attitudes toward tanning, despite the known risks, is a challenge for melanoma prevention[11,18].

Theoretical models

Theoretical models have been used to underpin interventions promoting sun protection behaviors, namely the Transtheoretical Model (TTM), the Theory of Planned Behavior (TPB), and the Health Belief Model (HBM).

The TTM is a model of intentional behavior change, composed of five stages: precontemplation, contemplation, preparation, action, and maintenance.

Yusufov et al. found that individuals successful in maintaining behavior consistently use more processes of change, like increasing awareness and stimulus control than those who relapse or do not change[14].

The TPB argues that behavior is determined by behavioral intention.

Durand et al. refers to the use of TPB; however, they do not provide detailed information about practical application in the study, which limits the assessment of its effectiveness[11].

The HBM seeks to explain and predict health behaviors based on individual beliefs and perceptions about disease and the benefits of preventive action.

Variables such as age, gender, and previous experiences also influence these perceptions. Aleo et al. applied a questionnaire based on the HBM to assess perceived melanoma risk, concern, knowledge, and protective behaviors, with the data used for social marketing[19].

The HBM emphasizes that factual knowledge alone is insufficient. Effective interventions must act on perceptions, motivate action, and provide realistic strategies for adopting healthy behaviors.

Practical implications

Across studies, BC interventions seem to improve sun-protective behaviors, particularly sunscreen use and awareness of melanoma risk.

Educational and counseling interventions demonstrated variable effectiveness in translating knowledge into sustained behavior change. Several studies highlighted that increased knowledge alone does not necessarily reduce risky behaviors, especially in populations with persistent positive attitudes toward tanning.

Sun protection campaigns could therefore go beyond generic messages focused exclusively on oncological risks. The inclusion of arguments related to the aesthetic effects of sun exposure, such as photoaging, may also prove effective, especially among younger population groups who may value esthetics more or who have lower levels of education.

Future interventions can, therefore, focus on modifying positive attitudes toward tanning, as well as transforming the social norms that promote it.

The promotion of regular and daily use of sunscreen should also be a priority in public health strategies, as it is a cost-effective measure that contributes significantly to the reduction of melanoma incidence.

It is also important to recognize that patterns of sun exposure vary according to lifestyle and occupational context. Effective prevention campaigns should be tailored to specific populations, for example, taking into account that outdoor workers exhibit different risk behaviors than tourists engaging in more recreational outdoor activities.

Furthermore, it is necessary to support not only the initial adoption but also the maintenance of protective behaviors. The application of theoretical models can be useful in this context, highlighting the importance of processes of change which contribute to the sustained maintenance of preventive behaviors. Applying these models in practical interventions offers a more personalized and effective approach to behavior modification, especially if perceptions of risk, perceived barriers, and individual incentives for behavior change are taken into account[20].

Raising population awareness requires an integrated effort and approach among different stakeholders. We must recognize that health professionals play a fundamental role in educating the population about the risks of sun exposure. It is equally important to ensure that future health professionals are properly prepared to inform and guide the population, ideally through strategies adapted to individual characteristics.

Overall, BC interventions show moderate-strength evidence for improving preventive behaviors, though long-term adherence and clinical outcomes remain insufficiently studied.

BC and technology, mobile applications, online interventions, and multimedia resources (T)

Regarding the use of technology in primary prevention, the most recurring themes include sending text messages to mobile phones (SMS), smartphone applications (apps), and web-based interventions and multimedia resources.

Text messages (SMS) appear to be a flexible way to support the promotion of sun protection behaviors. Studies address their use for sending reminders or educational messages related to sun protection or skin self-examination. They often include elements of personalization based on participant characteristics, such as gender, risk factors, and previous history of sunburns. Some studies also evaluate the use of interactive messages, requiring participant response or interaction with links to websites, and the effectiveness of different sending frequencies (daily, weekly, and monthly).

Horsham et al. suggest that text message interventions could lead to an increase in sun protection and a decrease in sunburns among young adults, with effects lasting up to 6 months after follow-up[21].

On the other side, Youl et al. demonstrated that SMS intervention did not appear to have a significant effect on the proportion of participants reporting sunburns, although all groups reported decreasing rates.

Horsham et al. and Youl et al. found that the acceptability of these interventions is generally high, with most participants reading the messages sents; therefore, the role of text message interventions in melanoma prevention is promising[21].

Horsham et al. also found a preference for interactive messages, which require a response from the recipient, and an ideal frequency of three messages per week.

It would be interesting to understand whether offering the individual option to personalize reminders, frequency, or message reception time influences primary prevention behaviors, as well as whether messages with positive reinforcement responses, such as praise, requiring feedback, and responses from participants, could be truly more effective[21].

Interestingly, it was observed that text messages may encourage conversations about sun protection among participants and their friends or family, involving a significant proportion of the sample[21,22].

Regarding smartphone applications, they can include features such as notifications or reminders for skin self-monitoring and provide prevention and awareness information. For example, the SunSmart Global UV app provides sun protection alerts based on real-time and forecast UV levels, adapted to the user's location.

Some studies have also focused on online interventions and multimedia resources (computer-based interactive programs) to provide information and promote behavioral changes. Manne et al. found that the online intervention "mySmartSkin" in melanoma survivors was associated with a beneficial impact on skin self-examination and sun protection behaviors, with some effect over time[23].

Glazebrook et al. demonstrated that the interactive program "Skinsafe," which uses images, animation, and sound to reinforce learning, reported positive changes in at least one photoprotective behavior, most frequently related to the use of protective clothing, although the average study quality was considerate moderate[24].

Bowen et al., in 2017, found that the web intervention "Suntalk" for families of melanoma survivors favorably changed the frequency of communication about cancer risk among family members. It was also linked to increased levels of protection behaviors, although website usage frequency was not associated with outcomes[14].

In addition, technology is being used in the development of new risk assessment tools that can be implemented in primary care settings, for example, through tablets in waiting rooms, to provide personalized prevention strategies. Teledermatology and UV sensors that can be used in clothing are other technologies with potential to improve melanoma prevention and early detection, although evidence on their effectiveness and implementation is still limited, according to Singh et al.[20,25].

Technology-based approaches demonstrated high acceptability and modest short-term improvements in sun-protective behaviors. Evidence regarding SMS interventions was mixed: some studies reported reductions in sunburns and improved protection behaviors, while others showed no significant differences compared to controls.

Web-based and multimedia interventions appeared beneficial in specific populations, such as melanoma survivors and high-risk individuals, particularly for skin self-examination and communication about risk. However, engagement levels varied.

Overall, the evidence for technology-based interventions can be considered promising but heterogeneous, with outcomes largely dependent on user engagement and population characteristics. Equity and accessibility remain key limitations.

BC and the provision of genetic or personalized information on individual risk of developing melanoma (G)

The provision of genetic or personalized information on individual risk is also explored as a potential strategy to improve melanoma prevention.

This approach is essentially based on the analysis of common genetic variants, such as those in the *MC1R* gene, or on the use of polygenic risk scores based on multiple genes. The goal is to communicate risk individually to participants, often through educational materials and counseling. Ultimately, the use of this personalized information aims to promote more effective prevention and detection behaviors by increasing risk awareness.

Several studies seek to evaluate whether communicating personalized risk effectively leads to changes in sun protection and detection behaviors.

Lacson et al. demonstrated self reported improvements in specific prevention and detection behaviors, particularly among participants identified as having higher risk, including those with a family history of melanoma. Reported behaviors included increased use of sunscreen, increased frequency of professional skin examinations, increased frequency of skin self-examinations, and increased use of sunglasses and protective clothing[26].

On the other hand, Lacson et al. report that the personalized intervention did not have a significant impact on reported preventive behaviors among participants at medium or low risk, suggesting that the information may be more relevant for high-risk individuals[25].

Smit et al. and Lacson et al. demonstrated the feasibility and acceptability of the population in receiving personalized information on genomic melanoma risk. However, Hay et al. reported heterogeneous results regarding interest in and adherence to genetic testing

based on demographic and socioeconomic factors, such as ethnicity and education level, indicating that non-Hispanic white and more educated populations could be more likely to show interest[9,26,27].

Studies evaluating the communication of personalized or genetic melanoma risk show therefore mixed results. While high-risk individuals demonstrated some potential improvement in preventive and detection behaviors, medium and low risk groups showed little or no behavioral change.

Most studies state that personalized risk communication was feasible and did not increase anxiety or risk behaviors[28]. However, differential interest and uptake across socioeconomic and ethnic groups raise concerns about equitable implementation. Altogether, the evidence suggests selective effectiveness, which may indicate more benefit among high-risk populations, but limited impact at the population level.

Chemoprotective agents (AQ)

Some studies also consider chemoprevention as a promising approach in melanoma prevention, which involves the use of drugs or natural agents with the aim of reducing the risk of developing the disease.

Pulumati et al. and Yan et al. investigated the chemopreventive potential of aspirin and other non-steroidal anti-inflammatory drugs in the context of cutaneous melanoma. The authors explored the possible biological mechanisms underlying the action of aspirin, namely the inhibition of the nuclear factor kappa B signaling pathway and cyclooxygenase (COX) enzymes, especially COX-2, whose expression has been associated with malignant cell progression[29,30].

The studies highlight the need for more large-scale prospective studies with diverse populations and well-structured methodologies, which would allow clarification of this relationship and provide more robust clinical guidance.

On the other hand, Serini et al. highlight the potential of long-chain n-3 polyunsaturated fatty acids (LC n-3 PUFAs), consumed through the diet, in melanoma prevention. These fatty acids appear to exert some beneficial effects when used in combination with conventional therapies or as vehicles for drug delivery, being therefore more relevant for treatment or for enhancing existing therapeutic efficacy. Specifically in melanoma, LC n-3 PUFAs may inhibit tumor cell growth and induce apoptosis, mechanisms that may also be associated with the reduction of COX-2 expression[5].

The hypothesis that LC n-3 PUFAs could act as chemopreventive agents for melanoma is based on results obtained in preclinical studies, as well as preliminary epidemiological observations. These data are complemented by the identification of multiple molecular mechanisms through which these compounds may exert a sustained protective effect against melanoma development. However, it is important to emphasize that the chemopreventive potential of LC n-3 PUFAs still requires validation through rigorously conducted human studies to confirm the benefits suggested by initial research.

Therefore, evidence supporting chemoprevention remains weak and inconclusive. While aspirin and LC n-3 polyunsaturated fatty acids have biologically plausible mechanisms and show promise in preclinical studies, human data are inconsistent and insufficient to support clinical recommendations. Current findings highlight the need for rigorously designed prospective studies before chemoprevention can be considered a viable preventive strategy.

Limitations and suggestions

Among the four categories, BC interventions currently have the strongest evidence base, particularly for promoting sunscreen use, whereas T and G interventions show context-dependent effectiveness and CQ strategies remain largely experimental. Across all categories, most outcomes rely on self-reported behaviors rather than long-term clinical endpoints, limiting conclusions regarding melanoma incidence and mortality reduction.

Future research should prioritize standardized outcome measures, and equitable intervention strategies that address social norms and behavioral maintenance rather than knowledge alone.

The use of standard erythemal doses measured by devices can assess sun exposure more accurately than self-reporting. Changing the data collection method from in-person interviews to online questionnaires may also potentially reduce social desirability bias.

It would also be interesting to study younger populations, who appear more prone to risk behaviors, and male populations, who are underrepresented in several studies. Additionally, populations with lower educational levels should be considered, along with how to personalize interventions for different educational levels.

In older populations, it would be valuable to conduct more studies on how to change behavioral habits in this age group, since providing personalized genetic information did not appear to be effective, nor did increasing general knowledge, according to Crowder et al.[31].

Melanoma prevention requires a multifaceted approach; therefore, training general practitioners to identify higher-risk groups and provide more effective personalized interventions would be valuable. However, given that some of the main barriers to implementing primary prevention activities in primary healthcare include limited consultation time and competing demands on professionals, there is a need for future research on the feasibility and acceptability of integrating personalized, risk-based prevention strategies, and early skin cancer detection into primary care models.

Most studies have a follow-up period of up to 1 year, which may not be sufficient to assess the effectiveness and maintenance of sun protection behaviors. Studies with longer follow-up periods would therefore be important in the future to evaluate the efficacy of primary prevention strategies.

Conclusion

Melanoma prevention is a global public health priority due to its high incidence and mortality, particularly in populations with higher sun exposure. The literature addresses various primary prevention strategies, including behavioral counseling and health education, the use of technology, the provision of genetic information, and the exploration of chemoprotective agents. Interventions aimed at modifying risk behaviors, combined with awareness strategies and innovative technologies, can contribute significantly to reducing melanoma incidence, especially when tailored to the specific needs of population subgroups.

On one hand, behavioral counseling, education, and population awareness to adopt sun protection behaviors have been shown to be crucial components of prevention strategies. Regular use of sunscreen remains the most accessible and effective preventive measure for primary melanoma prevention, and studies indicate that it can significantly reduce melanoma incidence, representing a cost-effective public health strategy.

Additionally, education and awareness, whether through printed or digital educational campaigns, have an important impact on modifying behaviors. However, the effectiveness of these interventions may be limited by factors such as individual risk perception and cultural attitudes, such as the a esthetic value placed on tanning.

The use of theoretical models, such as the TTM and the HBM, in the design of behavioral change strategies has proven fundamental for understanding the psychological processes involved in adopting sun-protective behaviors.

Incorporating technology into melanoma prevention interventions has also proven to be a promising strategy, particularly among young populations with access to technology. Sending text messages (SMS) and developing mobile applications promote preventive behaviors, such as sunscreen use, skin self-examinations, and adoption of real-time photoprotection practices tailored to user characteristics and environmental conditions.

Multimedia resources, such as interactive online websites, have also demonstrated utility in promoting health literacy and improving adherence to protective behaviors, such as performing skin self-exams. Through visual and interactive elements, these tools contribute to better understanding and retention of information by the population.

Subsequently, the provision of personalized information about genetic risk for melanoma is an emerging area of research with great potential to improve prevention. However, the effectiveness of this approach appears limited in individuals with medium or low risk, and adherence may be influenced by demographic and socioeconomic factors. The provision of genetic information should be carried out cautiously to avoid low-risk individuals becoming complacent about preventive measures.

Finally, chemoprevention, especially the use of chemoprotective agents such as aspirin, has been explored in some studies, although the results remain inconclusive and do not allow for clear practical recommendations.

It is also important to emphasize that successful implementation of melanoma prevention strategies requires an integrated approach. Therefore, collaboration between healthcare professionals, researchers, and public health officials is essential in developing targeted campaigns and interventions tailored to the specific characteristics of each population group.

Reducing melanoma incidence requires collective responsibility and continuous, multifaceted effort. Future studies should focus on larger participant numbers and longer follow-up periods to determine the best and most effective strategies for behavioral change that are demonstrably long-lasting and sustained, ultimately reflecting a real decrease in melanoma incidence.

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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. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence (AI). The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

Supplementary data

Supplementary data are available at DOI: 10.24875/PJDV.25000077. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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REVIEW ARTICLE

Unveiling leprosy through machines: a review of artificial intelligence in a neglected tropical disease

Revelando a lepra através de máquinas: uma revisão da inteligência artificial numa doença tropical negligenciada

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Abstract

Leprosy persists as a major public health challenge in many areas of the world, with nearly 200,000 new cases reported annually despite the success of multidrug therapy. Timely diagnosis remains pivotal to preventing disability and interrupting transmission; however, dependence on clinical acumen and variable diagnostic infrastructure continues to impede early detection. Recent advances in artificial intelligence (AI) herald transformative potential across diagnostic, classification, monitoring, and epidemiological dimensions. Convolutional neural networks and hybrid deep learning architectures have demonstrated diagnostic accuracies exceeding 90% in differentiating leprosy from phenotypically similar dermatoses, while explainable AI frameworks enhance interpretability and clinician confidence. Machine learning algorithms leveraging registry and questionnaire-based data enable reliable classification of paucibacillary and multibacillary forms, facilitating community-level triage. Integration of biochemical, spectroscopic, and geospatial analytics further supports therapeutic monitoring and targeted surveillance. Persistent challenges include limited dataset diversity, insufficient external validation, and unresolved ethical issues surrounding data governance, bias, and privacy. Future directions lie in federated learning, multimodal integration, and patient-centric digital platforms. The fusion of computational precision with human compassion may ultimately redefine early detection and accelerate global leprosy elimination.

Keywords: Leprosy. Artificial intelligence. Neglected tropical disease. Machine learning.

Resumo

A lepra persiste como um grande desafio de saúde pública em muitas partes do mundo, com quase 200.000 novos casos reportados anualmente, apesar do sucesso da poliquimioterapia. O diagnóstico atempado continua a ser fundamental para prevenir a incapacidade e interromper a transmissão; no entanto, a dependência da experiência clínica e a infraestrutura de diagnóstico variável continuam a dificultar a deteção precoce. Os recentes avanços na inteligência artificial (IA) anunciam um potencial transformador nas dimensões de diagnóstico, classificação, monitorização e epidemiologia. As redes neuronais convolucionais e as arquiteturas híbridas de aprendizagem profunda demonstraram uma precisão diagnóstica superior a 90% na diferenciação entre lepra e dermatoses fenotipicamente semelhantes, enquanto as estruturas de IA explicáveis potenciam a interpretabilidade e a confiança do médico. Os algoritmos de aprendizagem automática que utilizam dados de registos e questionários permitem a classificação fiável de formas pauci- e multibacilares, facilitando a triagem a nível comunitário. A integração de análises bioquímicas, espectroscópicas e geoespaciais apoia ainda mais a monitorização terapêutica e a vigilância dirigida.

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Os desafios persistentes incluem a diversidade limitada dos conjuntos de dados, a validação externa insuficiente e questões éticas não resolvidas relacionadas com a propriedade e tratamento dos dados, o enviesamento e a privacidade. As direções futuras apontam para a aprendizagem federada, a integração multimodal e as plataformas digitais centradas no doente. A fusão da precisão computacional com a compaixão humana pode, em última análise, redefinir a deteção precoce e acelerar a eliminação global da lepra.

Palavras-chave: Lepra. Inteligência artificial. Doença tropical negligenciada. Aprendizagem de máquina.

Introduction: old scars, new codes

Leprosy, an affliction that once shaped empires and exiles, continues to cast a long shadow across the twenty-first century in several areas of the world. Despite the remarkable decline in prevalence following the introduction of multidrug therapy (MDT) in the 1980s, approximately 200,000 new cases are reported annually worldwide, disproportionately affecting the most marginalized communities[1,2]. Diagnosis still rests largely on the trained human eye: recognition of hypopigmented or erythematous patches with sensory loss, thickened nerves, or the presence of acid-fast bacilli on slit-skin smear[1]. Yet these signs often arrive late, when neural damage and stigma have already taken root.

The World Health Organization (WHO) has repeatedly emphasized the urgency of accelerating diagnosis and breaking transmission[1]. However, dwindling clinical expertise, particularly in regions where leprosy incidence is now sporadic, has deepened the diagnostic gap[3]. Here lies the quiet promise of artificial intelligence (AI): an ensemble of algorithms capable of learning patterns beyond human perception, translating the language of skin, nerve, and data into signals that could shorten the diagnostic odyssey.

Recent years have witnessed a burgeoning interest in digital health interventions for neglected tropical diseases (NTDs), with AI at their frontier[4,5]. While melanoma, psoriasis, and atopic dermatitis have already been subjects of robust machine learning (ML) pipelines, leprosy has only begun to find its place in this digital landscape[6]. What follows in this review is both a cartography and a critique: a mapping of where AI has already walked alongside leprosy, and where its footprints remain faint.

AI primer: teaching machines to see

AI, at its core, is the science of teaching machines to see patterns where humans falter. It thrives on three intertwined streams: ML, which allows computers to learn from data without explicit programming; deep learning (DL), which uses multilayered neural networks to extract hierarchies of meaning; and convolutional neural networks (CNNs), architectures inspired by the visual cortex that excel in recognizing features within images[4].

In dermatology, these architectures have become particularly powerful. A CNN can parse the subtle borders of a melanoma, distinguish the erythema of eczema from psoriasis, or map acne severity with accuracy rivalling expert clinicians[4]. This success provides a fertile precedent for NTDs, where diagnostic expertise is scarce and stigma delays recognition.

The learning process of AI can be explained through an analogy drawn from animal behavior. Consider a deer named *Shakuntala*, whose survival depends on learning from her surroundings. Early in life, *Shakuntala* learns by repetition. Certain sounds or movements are repeatedly followed by danger, while others are harmless. Over time, she learns to respond correctly, even though she does not know the reason behind each signal. This is similar to ML, where systems learn by repeatedly seeing labeled examples.

With experience, *Shakuntala's* learning becomes more advanced. She no longer depends on a single sign. Instead, she combines several cues at once, such as changes in sound, movement, and wind direction. Looking at these cues together allows her to make better decisions. This reflects DL, where models learn complex patterns by analyzing large amounts of data rather than following fixed rules.

When observing her environment, *Shakuntala* does not take in everything at once. She notices small details first, such as movement at the edge of vision or contrast among leaves, and then combines them to understand the larger scene. CNNs work in a similar way by analyzing small parts of an image and gradually combining them to reach an accurate conclusion.

In dermatology, disease recognition is fundamentally visual; the defining "identity" of a condition lies in the morphology of the lesion, including its shape, border characteristics, color variations, and surface texture. AI systems are trained to interpret these same visual cues. Through exposure to large, annotated image datasets, AI algorithms learn to differentiate the characteristic

features of leprosy from those of other dermatoses, much like how a child learns to recognize familiar faces within a family through repeated observation and pattern recognition[4].

For leprosy, the biological canvas is both complex and fragile: hypopigmented or erythematous patches, nodules, infiltrated skin, and the silent thickening of nerves. These lesions are visual, yet their patterns are subtle, overlapping with other dermatoses such as vitiligo, pityriasis alba, tinea, and even eczema[6]. The promise of AI is that it can distil thousands of such images into clusters of recognition, seeing regularities invisible to the human gaze.

But AI is not merely an "eye." It can be trained to integrate multimodal data: clinical metadata (age, sex, geography), sensory test results, slit-skin smears, histopathological slides, or even molecular signatures[7]. This layered approach mirrors the Ridley-Jopling spectrum[2], where disease expression exists along a continuum rather than in binaries. Algorithms can learn the "grey zones" that human classification often struggles with.

Thus, AI in leprosy begins not as a replacement for the clinician but as a new interpreter of signals: signals etched into skin, whispered through nerves, and translated into code.

Diagnosis: spotting the lesions we miss

Diagnosis has always been leprosy's first betrayal: the faint hypopigmented patch mistaken for pityriasis alba, the tingling nerve dismissed as fatigue, the nodule that waits too long before being named. Even expert clinicians may falter when early signs mimic more common dermatoses. AI offers a new lens, not a perfect one, but one that does not tire, forget, or look away.

Two recent systematic reviews chart the landscape. Fernandes et al. synthesized 21 studies and found that most models, built on CNNs, achieved high diagnostic accuracy but suffered from limited datasets and poor external validation[6]. De Andrade et al. expanded the view to 30 studies, highlighting CNNs, support vector machines (SVMs), and neural networks trained on diverse image sets, again promising, but hindered by heterogeneity[8].

Dermoscopy, long considered an extension of the dermatologist's eye, is now becoming the bridge between human perception and machine vision. In a multicentric study, Ankad et al. showed that distinct dermatoscopic patterns, including distorted pigment networks (90.6%), focal white areas (75.5%), and reduced follicular openings (81.1%), could reliably indicate leprosy and its spectral variations, providing non-invasive diagnostic cues[9]. Parallel advances in AI have already transformed dermoscopic analysis in other skin diseases. Olayah et al. trained hybrid CNNs (AlexNet-GoogLeNet-VGG16) to interpret dermoscopy images with near-human precision (accuracy 96.1%)[10]. Together, these findings suggest that integrating dermatoscopic imaging into AI pipelines could enable early, non-invasive identification of leprosy lesions, where pigment, texture, and vascular clues become quantifiable patterns for machines to learn.

Among primary studies, Barbieri et al. demonstrated the AI4Leprosy system, combining clinical photographs with metadata to achieve over 90% accuracy (area under curve (AUC) of 96.46%)[11]. Beesetty et al. used few-shot learning on only 368 images, suggesting that even with scarce data, algorithms can reach ~73% accuracy[12]. Baweja et al. went further, introducing "LeprosyNet," an explainable CNN architecture. By visualizing which parts of the lesion influenced classification, their model not only reached 98% accuracy but also opened the "black box" of AI to clinicians[13].

Together, these studies (Table 1) suggest that AI can already "see" the lesions we miss, though for now, only in curated datasets. The real challenge is not accuracy *in silico*, but translation into crowded clinics and rural outposts where stigma and silence still prevail.

Across the five key resources[6,8,11-13], AI models for leprosy diagnosis were primarily trained on curated datasets of visible skin lesions, including patches, plaques, macules, papules, and nodules, captured under standardized imaging conditions or sourced from public repositories. Only Barbieri et al.[11] integrated clinical and sensory metadata (e.g., loss of thermal sensation, paraesthesia, scaling), whereas others like Beesetty et al.[12] focused purely on image-based pattern recognition. No study included leprosy reactions (Type 1 or Type 2) or neural leprosy in training datasets, nor did they analyze AI's ability to distinguish reactional states. Thus, while AI systems can now differentiate "leprosy-like lesions" with high accuracy in silico, their clinical input variables remain largely confined to morphological and sensory features of primary lesions, not inflammatory or reactional phases.

Classification: from Ridley-Jopling to algorithms

The Ridley-Jopling spectrum, with its polar forms (tuberculoid at one end, lepromatous at the other) and

Table 1. Diagnostic applications of AI in leprosy: evidence from recent studies

Study	Dataset	AI method	Performance	Contribution
Fernandes et al. (JCM SLR)[6]	21 studies	Mostly CNNs	Accuracies generally high	First pooled evidence, highlights small datasets
De Andrade et al. (PLOS SLR)[8]	30 studies	CNNs, SVM, NN	Promising, heterogeneous	Most comprehensive systematic review
Barbieri et al. (Lancet Reg Health)[11]	1,229 images + 585 metadata	CNN + logistic regression	90% accuracy, AUC 0.96	Proof-of-concept, strong real-world dataset
Beesetty et al. (IJL)[12]	368 images	Few-shot learning CNN	~73% accuracy	Shows feasibility with minimal data
Baweja et al. (IEEE)[13]	Custom dataset	LeprosyNet (explainable CNN)	98% accuracy	Introduces explainability via Grad-CAM

AI: artificial intelligence; CNNs: convolutional neural networks; SVMs: support vector machines; NNs: neural networks; AUC: area under curve; Grad-CAM: gradient-weighted class activation mapping.

the borderline states in between, has long been the compass of leprosy classification[2]. Yet, in practice, the spectrum is often blurred. Clinical assessment can be subjective; slit-skin smears and histopathology, while useful, remain inconsistently available. This diagnostic ambiguity between paucibacillary (PB) and multibacillary (MB) disease carries therapeutic consequences, since treatment regimens depend on classification.

AI is now being trained to navigate these grey zones. De Souza et al. used registry data from Brazil's SINAN system (National Notifiable Diseases Information System) to develop a mobile health app that applies ML algorithms (random forest, decision trees, logistic regression) to classify patients as PB or MB. Their best-performing model achieved 94% sensitivity and 87% specificity, suggesting AI could assist even non-specialist health workers in the field[14].

Simões et al. developed the ML for Leprosy Suspicion Questionnaire Screening, applying SVMs and other models to patient-reported data. Their SVM classifier reached 85.7% sensitivity and 69.2% specificity, a performance notable for using only a short, 14-item questionnaire[15].

Each of these algorithms brings distinct strengths. Decision trees split data into simple yes/no questions, like a flowchart, making them easy to interpret. Random forests combine many such trees to reduce errors and improve stability. Logistic regression uses probability to separate categories, a more statistical approach. SVMs work differently: they draw a "boundary" in the data that best separates PB from MB cases, even when the differences are subtle[4].

These examples (Table 2) show that AI is not limited to images; it can also classify through metadata, questionnaires, and registry inputs. Just as Ridley and Jopling once gave clinicians a framework to interpret leprosy's variability, algorithms may provide new maps: not to replace judgment, but to refine it, especially where expert dermatologists are scarce.

Monitoring: pixels that remember healing

Treatment in leprosy is measured not only in the swallowing of MDT pills but in the slow fading of patches, the softening of nodules, and the return or absence of sensation. Yet clinicians know this trajectory is often uncertain: lesions can persist, relapse may masquerade as reaction, and bacilli can linger long after apparent cure. Here, AI has begun to step in, offering a way to quantify what the human eye cannot reliably measure.

In a recent study, Novack et al.[16] developed and validated a diagnostic method based on Fourier-transform mid-infrared spectrophotometry (MIR-FTIR) combined with chemometric modeling for the early detection and therapeutic monitoring of leprosy. Using plasma samples from untreated patients, post-treatment patients, and healthy controls, the authors applied principal component analysis and partial least-squares discriminant analysis to classify spectra with sensitivities and specificities approaching 97-100%. Although the study demonstrated excellent diagnostic accuracy, the authors did not specify which spectral bands or biochemical constituents contributed most to group separation. Thus, while the method shows promise as a low-cost, non-invasive biochemical fingerprinting approach, further work is needed to identify the specific molecular alterations underlying the spectral differentiation between active, treated, and healthy states of leprosy.

Table 2. Classification attempts of leprosy using AI methods

Study	Dataset/Input	AI method	Performance	Contribution
De Souza et al. (JMIR)[14]	Brazil SINAN registry data	Random forest, decision tree, logistic regression	Sensitivity 94%, specificity 87%	PB versus MB classification in mHealth app
Mendonça Ramos Simões et al. (Sci Rep)[15]	14-item questionnaire (LSQ)	SVM, decision trees, ensemble models	SVM: 85.7% sensitivity, 69.2% specificity	Demonstrated AI screening via questionnaires

PB: paucibacillary; MB: multibacillary; SVMs: support vector machines; LSQ: leprosy suspicion questionnaire; SINAN: sistema de informação de agravos de notificação.

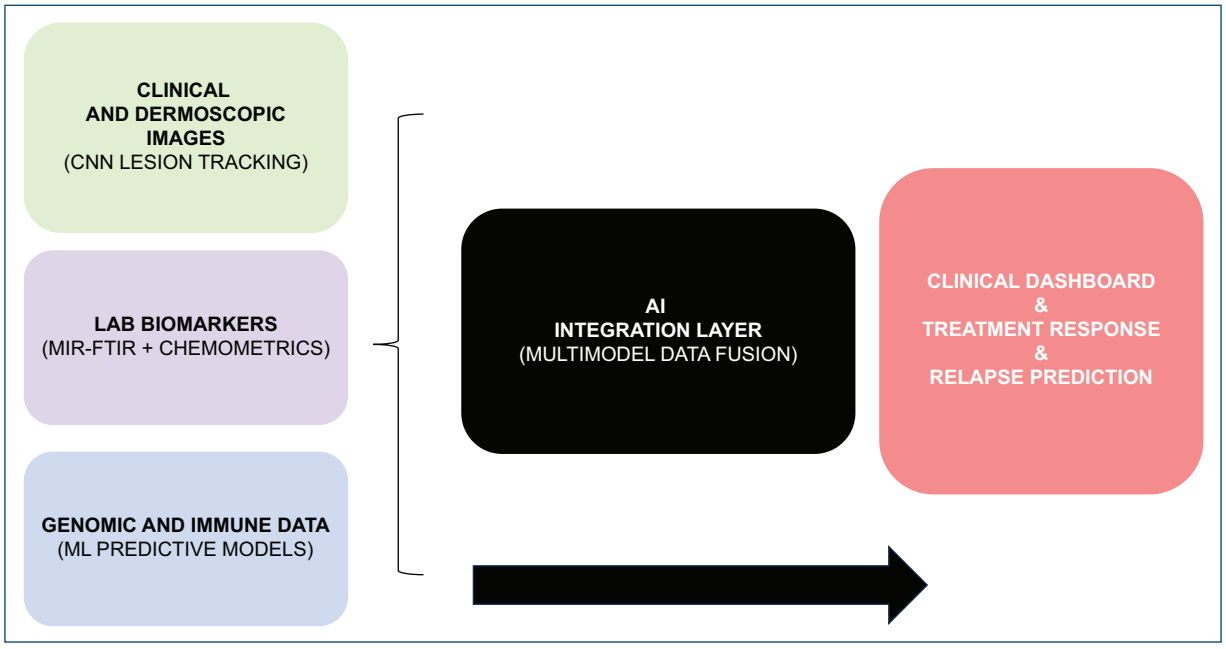

Figure 1. AI in monitoring leprosy treatment and relapse. AI: artificial intelligence.

Such techniques, while laboratory-based, suggest a low-cost, scalable method of monitoring therapy.

At the cellular level, AI could also integrate molecular and immunogenetic signatures. Li et al. have described how the host immune response and genetic regulation shape outcomes in leprosy, including vaccine responsiveness and susceptibility[7]. Linking such biomarkers with ML pipelines may enable predictive models that forecast relapse or resistance before they manifest clinically.

In practice, these tools (Fig. 1) can translate into a vision of longitudinal AI monitoring: a patient's clinical lesions and dermoscopic pattern photographed monthly, their plasma profiled periodically, their data compared not only to their own baseline but to global patterns learned across thousands of patients. Pixels remember what the eye forgets, and in doing so, they may prevent the cycle of relapse that has haunted leprosy control for decades.

Public health: epidemiology in the age of algorithms

If diagnosis is the intimate encounter between patient and clinician, epidemiology is the wide lens, mapping how disease moves through space and time. In leprosy, surveillance is hampered by stigma, underreporting, and limited resources. AI has begun to extend its reach into this domain, helping to chart "hidden geographies" of transmission.

Rodrigues da Motta and colleagues, writing in Leprosy Review, highlighted how AI-enhanced data systems can refine Brazil's surveillance, detecting clusters and predicting incidence in regions where official numbers understate the true burden[17]. Their letter underscored the urgency of integrating AI-driven predictive analytics with routine health information systems.

In Senegal, Deutsche Lepra- und Tuberkulosehilfe (DAHW) and Belle.ai partnered with the Ministry of Health to deploy smartphone-based AI tools that assist frontline workers in identifying leprosy and other NTDs in remote areas. The system includes a geographic information system platform to track infections and coordinate treatment. By enabling early detection and rapid referral to specialists, the project demonstrates the potential of AI to strengthen surveillance and patient care in low-resource settings[18].

At the global level, the WHO Skin NTD app, although not exclusively AI-driven, has introduced structured digital tools for frontline workers. When coupled with AI modules in development, it could enable syndromic surveillance across multiple NTDs, with leprosy as a key beneficiary[19].

Together, these examples show that AI's promise in public health lies not only in precision but also in scale: algorithms that can sift through scattered reports, images, and registries to generate maps, *"cartographies of contagion*," where human vision alone cannot reach.

Challenges: bias, bugs, and barriers

AI does not arrive in leprosy care as a neutral tool. It inherits the flaws of the datasets that train it, the inequities of the systems that deploy it, and the silences of the patients who remain unseen. The promise of precision must be weighed against the dangers of distortion.

A policy perspective from the Malaysian Health Technology Assessment Section concluded that evidence on AI applications for leprosy is very limited. Existing models are based on small pilot studies, use different input datasets, and lack sufficient validation for routine use. The report emphasized that larger studies with more representative data are needed before these tools can be reliably deployed in public health settings[20]. In leprosy, this gap is sharper: models trained on carefully curated images may misclassify in field conditions, where lighting, camera quality, and skin tone vary widely.

Deps et al. underscored another critical issue: the scarcity and uneven quality of data. Stigma and underdiagnosis already limit case reporting in many endemic regions, creating a large pool of undetected patients. Training AI models on narrow, geographically restricted datasets risks encoding local biases into tools intended for global use[21]. Moreover, explainability remains uneven. While some models (such as LeprosyNet) highlight the parts of a lesion that influenced the decision[13], others still provide results without showing their reasoning, making it difficult for clinicians to judge reliability.

Finally, there are ethical and legal questions: who owns lesion photographs captured in rural clinics? How are patients informed about AI use in their diagnosis? What safeguards exist if a model misclassifies a case? These questions remain unresolved but must accompany any technical advance.

Bias, bugs, and barriers are not abstract defects: they are reminders that AI in leprosy can amplify inequities if not designed, validated, and deployed with humility.

Future towards zero: neural nets and beyond

The aspiration of leprosy control has always been elimination, yet the road remains long. AI, if wisely shaped, could become part of that journey, not as a miracle cure, but as an amplifier of human effort.

Deps reminds us that AI's future in leprosy depends on equity of access, since models trained and validated only in high-resource centers will fail the peripheries where they are needed most[21]. Still, there are emerging strategies to bridge these divides. Federated learning, for instance, allows algorithms to be trained across multiple regions without pooling sensitive data, ensuring both privacy and diversity of input[22].

Multimodal approaches also loom on the horizon. Instead of relying solely on photographs, future models may combine clinical images, nerve function tests, genomic data, and immunological markers into unified predictions. Han and Solanki note that such integrations already show promise in other infectious dermatoses, suggesting leprosy may follow[4,5].

Another frontier lies in stigma reduction. By embedding AI within mobile tools that guide primary health workers, diagnosis may occur earlier and closer to home, reducing the delay that fuels disability and discrimination. In this way, the algorithm is not merely a classifier, but a silent advocate for patients who often remain unseen.

The path to zero will not be paved by neural nets alone, but by their careful alignment with public health

systems, ethical safeguards, and communities themselves. AI will not end leprosy, but it may help us imagine an end.

Sociocultural context: the human face of the machine

Beyond accuracy curves and performance metrics, AI in leprosy will always encounter the most enduring variable: people. Leprosy has never been just a bacterium in a nerve and the skin; it is stigma, silence, and centuries of exclusion. Any algorithm that ignores this context risks becoming irrelevant, or worse, harmful.

The Leprosy Exists blog captures this tension, documenting voices of those affected who express both hope and unease toward digital tools[23]. Some patients view AI-driven mobile apps as symbols of modernity, offering earlier recognition and dignity in care. Others worry that a camera capturing their lesion is yet another intrusion, another layer of labeling that reduces them to data points.

Clinicians, too, occupy an ambivalent space. While some see AI as a relief from diagnostic uncertainty, others worry it may erode the intimacy of clinical touch, replacing the careful palpation of a thickened nerve with the sterile scan of a smartphone.

Ultimately, the social fabric in which AI is introduced will shape its acceptance more than any technical detail. Trust must be built, not assumed. For AI in leprosy to succeed, it must carry not only precision but also compassion, remembering that behind every dataset is a face, a voice, a life.

Conclusion: algorithms as allies, not replacements

The history of leprosy is a history of persistence: of a bacterium that evades eradication, of a stigma that outlives cure, of a disease that still hides at the margins. AI enters this story not as a cure, but as a companion technology, a set of tools that may sharpen our gaze, extend our reach, and accelerate our responses.

The evidence we have reviewed demonstrates real progress. Algorithms can already distinguish lesions with accuracy rivalling specialists[6,8,11-13], classify patients into PB or MB with high sensitivity[12,13], and even monitor biochemical signatures of treatment response[7,16]. They can scan maps for clusters[17], guide mobile screening in rural campaigns[18], and sit inside WHO's global digital health frameworks[19]. These advances are neither trivial nor complete.

Yet AI must remain an ally, not an authority. Its limitations: data scarcity, uneven generalizability, and ethical uncertainties demand humility[21]. As the future unfolds, federated learning, multimodal integration, and patient-centered apps may bring us closer to the goal of leprosy eradication. However, no network, however deep, can replace the clinician's judgment, the health worker's trust, or the patient's story.

The most powerful vision, then, is not of algorithms replacing human care, but of algorithms walking beside it; steadying, amplifying, illuminating. In that alliance, the centuries-long shadow of leprosy may finally begin to fade.

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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. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence (AI). 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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ORIGINAL ARTICLE

Association of onychoscopic features and clinicomycological profiles in onychomycosis – a cross-sectional study

Associação de características onicoscópicas e perfis clinicomicológicos em onicomicose – um estudo transversal

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Abstract

Objectives: The primary objective of this study was to describe the onychoscopic patterns in patients with clinically suspected onychomycosis, and as secondary objectives, to explore the association of specific onychoscopic patterns with clinical types and the causative organisms. **Methods:** A cross-sectional study of 52 cases was conducted after obtaining ethical committee approval. All affected nails were subjected to clinical observation, onychoscopy, potassium hydroxide (KOH), and fungal culture. **Results:** We studied 34 females and 28 males, with a mean age of 47.2 ± 13 years, with clinically suspected toe and fingernail onychomycosis, of whom 44 (88.5%) had a confirmatory KOH or culture, mostly with the distal lateral subungual onychomycosis subtype and caused by *Candida, Fusarium,* and *Trichosporon*. Yellow or brown chromonychia, onycholysis, distal irregular termination, rough longitudinal white edge/trachyonychia, opacity, and linear white striae were the main onychoscopic findings in this and previous studies, whereas a shallow layered appearance was a new finding. Fungal melanonychia (9.6%) and blue–red globules (3.8%) were also identified in onychoscopy. There was some correlation between onychoscopic findings and the fungus cultured from the nail plate. **Conclusion:** Onychoscopy can be considered a non-invasive diagnostic tool to contribute to the diagnosis of onychomycosis, as KOH examination and culture have low sensitivity. Its correlation with the causative agent could lead to a better diagnosis and facilitate the right choice of the antifungal.

Keywords: Onychomycosis. Onychoscopy. Fungal culture. Chromonychia and onycholysis.

Resumo

Objetivos: O objetivo principal do presente trabalho foi a descrição dos padrões onicoscópicos em pacientes com suspeita clínica de onicomicose e secundáriamente correlacioná-los com padrões onicoscópicos específicos. os tipos clínicos de onicomicose, bem como os organismos causadores. **Métodos:** Estudo transversal de 52 casos, após aprovação do comitê de ética. Todas as unhas afetadas foram submetidas a observação, onicoscopia, KOH e cultura para fungos. **Resultados:** Neste estudo, foram incluídas 34 mulheres 28 homens, com idade média de 47.2 ± 13 anos, com suspeita clínica de onicomicose em dedos dos pés e unhas das mãos, dos quais 44 (88,5%) apresentaram KOH ou cultura confirmatória, a maioria com o subtipo DLSO e causada por *Candida, Fusarium* e *Trichosporon*. Achados onicoscópicos previamente descritos foram

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frequentemente observados (cromoníquia amarela ou castanha, onicólise, bordo áspero branco/traquioniquia, opaciade da lâmina ungueal e estrias brancas lineares), mas um aspecto com camadas superficiais foi um novo achado. Melanoníquia fúngica e glóbulos vermelho-azulados também foram identificados na onicoscopia. Houve alguma correlação entre os achados onicoscópicos e o fungo cultivado da lâmina ungueal. **Conclusão:** A onicoscopia pode ser utilizada como auxiliar diagnóstico não invasivo em casos em que exames como o exame de KOH e a cultura apresentam baixa sensibilidade. Sua correlação com a identificação fúngica pode levar a um melhor diagnóstico e facilitar o início da escolha correta dos agentes antifúngicos.

Palavras-chave: Onicomicose. Onicoscopia. Cultura fúngica. Cromoníquia e onicólise.

Introduction

Onychomycosis, a chronic fungal infection affecting finger and/or toenails, constitutes 18.40% of onychopathies and about 30% of mycotic cutaneous infections. It can be dermatophytic or non-dermatophytic in origin. Although not life-threatening, onychomycosis constitutes an important public health problem because of its high prevalence and associated negative consequences for patients, such as pain, and can potentially undermine work and social lives.

The five clinical types reported are distal lateral subungual onychomycosis (DLSO), superficial white onychomycosis, proximal subungual onychomycosis (PSO), endonyx onychomycosis (EO), and total dystrophic onychomycosis (TDO)[3]. The onychoscopic signs usually observed in onychomycosis are a jagged proximal edge with spikes, longitudinal striae, a ruined appearance, and longitudinal ridges along the nail bed. However, these findings are limited to DLSO and TDO[4]. Hoffman and Driver emphasized the need for a correct identification of the causative organism apart from diagnosing the clinical type of onychomycosis[5]. However, the relationship between onychoscopic and clinical features and the causative organism is unknown. Hence, the primary objective of the study was to describe onychoscopic findings in patients with clinically suspected onychomycosis. Secondary objectives were (A) to determine the association between specific onychoscopic features and the clinical types of onychomycosis; and (B) to determine the association between specific onychoscopic features and the causative organisms.

Participants and methods

This cross-sectional study was done in a tertiary care center in Pondicherry, where all the patients (n = 52) with a clinical diagnosis of onychomycosis attending the dermatology outpatient department in a tertiary care hospital were included. Patients on treatment with topical and systemic antifungals for the past 1 month or patients with other nail diseases, such as traumatic nail dystrophy, nail involvement in lichen planus, and psoriasis, were excluded. The sample size (52) was calculated assuming the prevalence of longitudinal striae and chromonychia on onychoscopy as 84% according to a study done by Abdallah et al.[6] with 10% precision and 95% confidence interval. The study was conducted after getting clearance from the research and ethics committees of the institute. (Ref no: IEC: RC/2020/102).

All the patients fulfilling the inclusion criteria were included in the study after obtaining informed consent. A complete history was taken, and a clinical examination was done. Onychoscopic examinations were completed using a Heine MINI 3000 dermoscope, and the findings were documented for all affected fingernails and toenails of each patient. Nail clippings were taken for potassium hydroxide (KOH) mount and fungal culture. When multiple nails were affected, clippings were taken from the most affected nail. KOH mounting was done by keeping a portion of the nail clippings overnight in 20% KOH solution and then examining them using light microscopy (×10 and ×40) for the presence of hyphae, pseudo-hyphae, and yeasts, as described by others[7].

Nail clippings were collected from the affected nails under sterile precaution after cleaningwith 70% alcohol on a sterile filter paper. The nails were clipped as proximally as possible from the free edge. he nail clippings were then inoculated into Sabouraud's dextrose agar containing ccycloheximide. The culture media were incubated at 25°C and 37°C for 4 weeks. Any growth on culture was identified by colony characters and microscopy using Gram's stain or Lactophenol-cotton blue preparation following the methods described by others[8]. The phenotypic tests done for the identification of yeasts were the germ tube test, CHROMagar, carbohydrate fermentation, and assimilation test. The

Table 1. Results of direct clinical examination

Findings	Frequency (n)	%
Nail plate crumbling	10	19.2
Nail plate pitting	7	13.2
Onycholysis	45	86.5
Onychomadesis	5	9.6
Nail dystrophy/ Loss of nail plate	46	88.4
Nail bed abnormality	7	13.5
Cuticle absent	22	42.3
Lunula absent	43	82.7
Subungual hyperkeratosis	15	28.8
Chromonychia (discolouration observed in the nail plates)	**Frequency (n)**	**%**
Yellow, brown	7	13.5
Yellow	19	36.7
Brown	22	42.3
Black	1	1.9
Green	2	3.8
White	1	1.9
Proximal nail fold involvement	15	28.8
Distal nail fold involvement	10	19.2

Table 2. Potassium hydroxide, culture, and fungus species were identified in the 52 samples collected

KOH and culture findings	n (%)
Results of KOH and nail fungal culture	
KOH positive	32 (61.5)
Culture positive	35 (67.3)
KOH + culture positive	21 (40.4)
KOH + culture negative	11 (21.1)
Organisms identified in the nail fungal culture	
Candida tropicalis	10 (19.2)
Candida albicans	5 (9.6)
Candida parapsilosis	1 (1.9)
Candida guilliermondii	2 (3.8)
Fusarium solani	7 (13.5)
Fusarium dimerium	1 (1.9)
Fusarium oxysporum	4 (7.7)
Cladosporium sphaerospermum	1 (1.9)
Trichosporon	3 (5.8)
Paecillomyces variotti	1 (1.9)
No organism growth	17 (32.7)

KOH: potassium hydroxide.

Table 3. Onychoscopic features in clinically typical onychomycotic nails

Onychoscopic features	n (%)
Chromonychia (discolouration observed in the nail plates)	
Yellow, brown	4 (7.7)
Yellow, black	3 (5.8)
Yellow, white	2 (3.8)
Yellow	17 (32.9)
Brownish yellow	1 (1.9)
Brownish black	5 (9.6)
Brown	14 (26.9)
Black	1 (1.9)
Green	2 (3.8)
White	1 (1.9)
Brownish white	2 (3.8)
Onycholysis types	
Distal onycholysis	11 (21.1)
Distal-lateral onycholysis	40 (76.9)
Proximal onycholysis	1 (1.9)
Other onychoscopic findings	
Opacity	31 (59.6)
Longitudinal white striae	31 (59.6)
Jagged proximal edge	28 (53.8)
Intermittent spiked pattern	23 (44.2)
Rough longitudinal white edge/trachyonychia	32 (61.5)
Linear edge	12 (23.1)
Distal irregular termination	36 (69.2)
Subungual hyperkeratosis	27 (51.9)
Dermatophytoma	5 (9.6)
Additional onychoscopic findings	
Fungal melanonychia	5 (9.6)
Blue red globules	2 (3.8)
Newer onychoscopic findings	
Shallow-layered appearance	24 (36.2)

molds were identified using Lactophenol cotton blue preparations from slide culture[9]. After 4 weeks, nail fungal culture reports were noted for each patient.

Data were analyzed using Microsoft Excel software 2017. Quantitative variables were presented in mean, standard deviation, total numbers, and percentages for each category. Student's t-test and the significance level of p value ($p < 0.05$) were employed.

Results

The study included 52 patients, 34 females (65.4%), 18 males (34.6%), with ages ranging from 20 years to 67 years (mean 47.2 ± 13 years), mostly between 41 and 50 years of age.

The clinical types identified in this study were, by order of frequency, DLSO (n = 38), TDO (n = 13), and PSO (n = 1). The other clinical types were not observed.

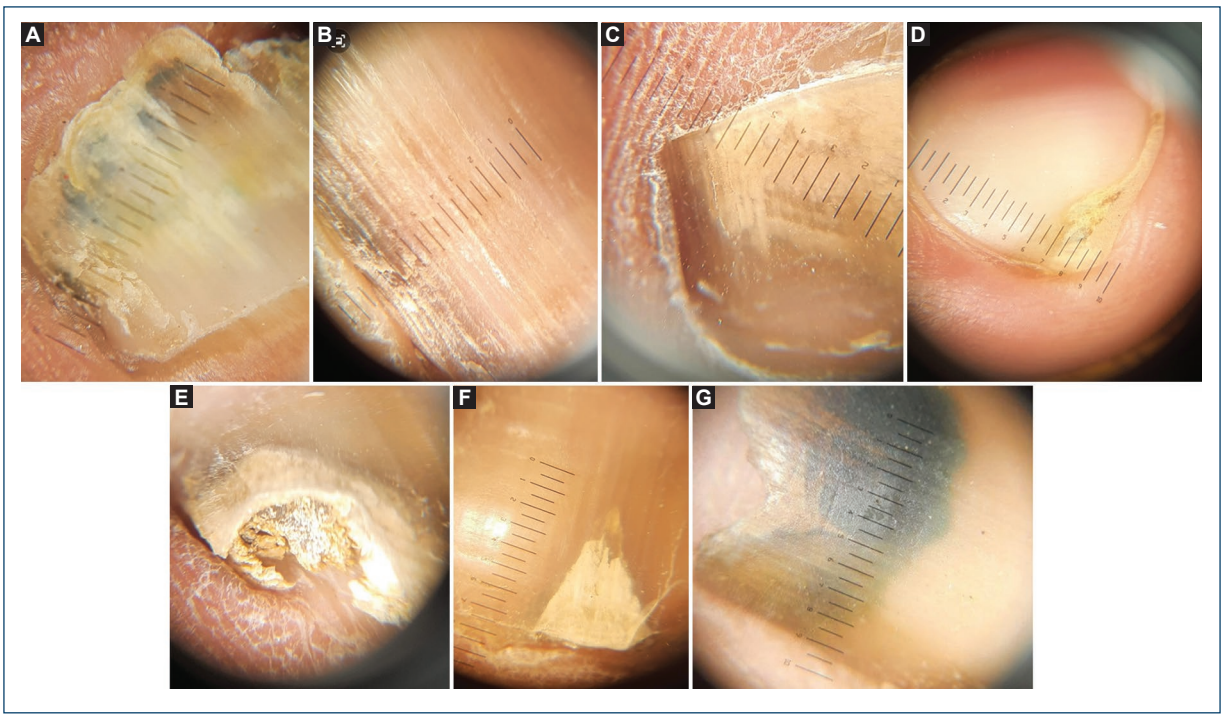

Figure 1. Onychoscopy images. **A:** onychoscopic image of the affected nail showing onycholysis in the distal and lateral areas of the nail plate seen in candidal onychomycosis. **B:** onychoscopic image of affected nail showing longitudinal white striae seen in candidal onychomycosis. **C:** onychoscopic image of affected nail showing jagged proximal edge. **D:** onychoscopic image of the affected nail showing a linear edge seen in potassium hydroxide (KOH) positive. **E:** onychoscopic image of affected nail showing subungual hyperkeratosis. **F:** onychoscopic image of affected nail showing dermatophytoma seen in KOH-positive onychomycosis. **G:** onychoscopic image of the affected nail showing fungal melanonychia.

The most common nails involved were fingernails, 55.7% (n = 29), compared to toenails, which were 36.5 % (n = 19). 7.8% (n = 5) had both finger and toenail involvement. The clinical examination findings are given in table 1.

KOH was positive in 32 patients (61.5%), and culture was positive in 35 out of 52 (67.3 %), and both were positive in 21 (40.4%), and both were negative in 6 patients (11.5%) (Table 2). The most common organism found in 18 specimens (34.6%) was *Candida* spp. (Table 2) which included *Candida tropicalis*, the commonest species (10 out of 18), *Candida albicans, Candida parapsilosis*, and *Candida guillermondii. Fusarium* was cultured in 12 patients, with *Fusarium solani* as the single 2nd most common organism grown in culture (14%). Other organisms were *Cladosporium sphaerospermum, Trichosporon*, and *Paecillomyces variotti*, accounting for 1.9%, 5.8%, and 1.9%, respectively (Table 2). No dermatophytes were found.

The onychoscopic features observed in the nails clinically diagnosed as onychomycosis were mostly chromonychia (n = 52; 100%), particularly a yellow or brown discoloration of the nail plate and onycholysis (n = 52; 100%) (Table 3). Chromonychia was better observed by onychoscopy than through the naked eye, with statistical significance of $p < 0.039$. The most common color was yellow (32.7%), but many different colors were observed on onychoscopy (Table 3). Onycholysis (Fig. 1A) was also better appreciated by onychoscopy (observed in all patients compared to 50 with naked eye), with distal lateral onycholysis as the topmost feature. The other onychoscopic findings were distal irregular termination (n = 36; 69.2%), rough longitudinal white edge/trachyonychia (n = 32, 61.5%), opacity of the nail plate (n = 31, 59.6%) and longitudinal white striae (n = 31, 59.6%) (Fig. 1B), jagged proximal edge (Fig. 1C) (n = 28; 53.8%) and intermittent spiked pattern (n = 23; 44%). Linear edge (Fig. 1D) as a non-specific feature of onychomycosis was observed in 23.1% patients. Subungual hyperkeratosis (Fig. 1E) observed

Table 4. Comparison of onychoscopic findings among different types of onychomycosis (DLSO, TDO, and others)

Onychoscopic findings	Comparison DLSO vs. others			Comparison TDO vs. others		
	DLSO (n = 38) (%)	Others (n = 14) (%)	p	TDO (n = 13) (%)	Others (n = 39) (%)	p
Chromonychia	38	14	-	13	39	-
Yellow	13 (34.2)	4 (28.6)	-	4 (30.8)	13 (33.4)	-
Yellowish brown	4 (10.5)	2 (14.3)	-	2 (15.4)	4 (10.3)	-
Yellowish black	2 (5.3)	1 (7.1)	-	1 (9)	2 (5.1)	-
Yellowish white	2 (5.3)	-	-	-	2 (5.1)	-
Brown	11 (28.9)	3 (21.4)	-	2 (18.2)	12 (30.8)	-
Brownish black	2 (5.3)	2 (14.3)	-	2 (18.2)	2 (5.1)	-
Black	1 (2.6)	-	-	-	1 (2.6)	-
Green	2 (5.3)	-	-	-	2 (5.1)	-
White	-	1 (7.1)	-	1 (9)	-	-
Whitish brown	1 (2.6)	1 (7.1)	-	1 (9)	1 (2.6)	-
Onycholysis	-	-	0.001	-	-	0.001
Distal-lateral	37 (97.4)	3 (21.4)	-	3 (23.1)	37 (94.8)	-
Total nail	-	10 (71.4)	-	10	-	-
Proximal	-	1 (7.1)	-	-	1 (2.6)	-
Opacity	23 (60.5)	8 (57.1)	1.000	7 (53.8)	24 (61.5)	0.747
Longitudinal white striae	21 (55.3)	10 (71.4)	0.353	9 (69.2)	22 (56.4)	0.523
Jagged proximal edge	21 (55.3)	7 (50)	0.764	6 (54.5)	22 (56.4)	0.541
Intermittent spiked pattern	16 (42.2)	7 (50)	0.755	6 (46.1)	17 (43.6)	1.000
Rough longitudinal white edge/ trachyonychia	21 (55.3)	11 (78.6)	0.200	10 (76.9)	22 (56.4)	0.324
Linear edge	10 (26.3)	2 (14.3)	0.475	2 (18.2)	10 (25.6)	0.706
Distal irregular termination	24 (63.2)	12 (85.7)	0.179	11 (84.6)	25 (64.1)	0.298
Subungual hyperkeratosis	15 (39.5)	12 (85.7)	0.004	11 (84.6)	15(38.5)	0.010

DLSO: distal lateral subungual onychomycosis; TDO: total dystrophic onychomycosis.

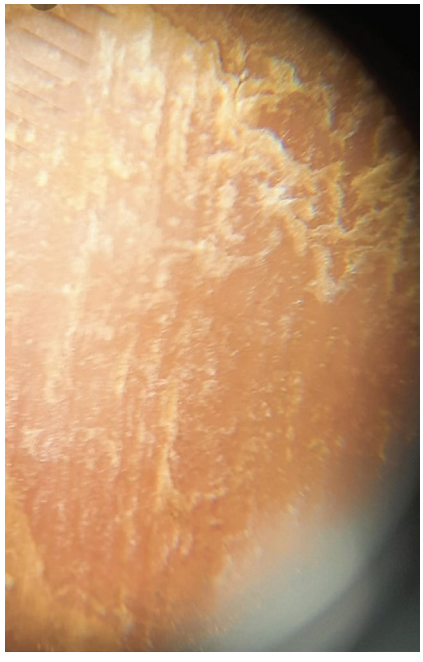

Figure 2. Onychoscopic image of the affected nail showing a shallow layered appearance of the nail plate.

in 15 patients on clinical examination and 27 on onychoscopy was not significant. A dermatophytoma (Fig. 1F) and fungal melanonychia (Fig. 1G) were observed in 5 patients each (9.6%) and blue-red globules in 2 (3.8%). A "shallow layered appearance" (Fig. 2) was a previously unreported onychoscopic finding observed in 24 patients (46.2%).

Table 4 shows a comparison of the onychoscopic findings in different cases of onychomycosis (DLSO, TDO, and PSO). The most common color in DLSO was yellow, followed by brown, but other types also showed yellow as the common color. Distal lateral onycholysis was observed in 37 (97.4%) patients with DLSO, which was statistically significant compared to other forms. Subungual hyperkeratosis was significantly less common in DLSO than in other types (p = 0.004). The other findings were non-contributory.

Subungual hyperkeratosis, observed in 11 out of 13 of TDO cases (84.6%), was significantly more frequent in this type compared to others (p = 0.010). Longitudinal white striae, intermittent spiked pattern, rough longitudinal white striae, and distal irregular termination were

Table 5. Comparison of the onychoscopic findings among organisms of culture

Onychoscopic findings	Comparison *Candida* vs. others			Comparison *Fusarium* vs. others		
	Candida (n = 18) (%)	Others (n = 34) (%)	p	*Fusarium* (n = 12) (%)	Others (n = 4) (%)	p
Chromonychia	-	-	-	-	-	-
Yellow	8 (44)	9 (26.5)	-	3 (25)	14 (35)	-
Yellowish brown	2 (11)	3 (8.8)	-	1 (8.3)	4 (10)	-
Yellowish black	1 (5.5)	2 (5.9)	-	1 (8.3)	2 (5)	-
Yellowish white	-	2 (5.9)	-	1 (8.3)	1 (2.5)	-
Brown	5 (27.5)	9 (26.5)	-	4 (33.3)	10 (25)	-
Brownish black	2 (11)	3 (8.8)	-	1 (8.3)	4 (10)	-
Black	-	1 (2.9)	-	1 (8.3)	-	-
Green	-	2 (5.9)	-	-	2 (5)	-
White	-	1 (2.9)	-	-	1 (2.5)	-
Whitish brown	-	2 (5.9)	-	-	2 (5)	-
Onycholysis	-	-	-	-	-	-
Distal-lateral	13 (72.2)	27 (79.4)	0.505	9 (75)	31 (77.5)	0.466
Total nail	4 (22.2)	7 (20.6)	-	2 (16.6)	8 (20)	-
Proximal	-	-	-	-	-	-
Opacity	11 (61.1)	20 (58.8)	1.000	6 (50)	25 (80)	0.512
Longitudinal white striae	8 (44.4)	23 (67.6)	0.141	6 (50)	25 (80)	0.512
Jagged proximal edge	6 (33.3)	22 (64.7)	0.043	10 (83.3)	18 (40)	0.024
Intermittent spiked pattern	9 (50)	14 (41.2)	0.571	8 (66.6)	15 (37.5)	0.102
Rough longitudinal white edge/trachyonychia	11 (61.1)	21 (61.8)	1.000	7 (58.3)	25 (20)	1.000
Linear edge	6 (33.3)	6 (17.6)	0.300	3 (25)	9 (40)	1.000
Distal irregular termination	9 (50)	27 (79.4)	0.056	9 (75)	27 (60)	0.733
Subungual hyperkeratosis	7 (38.8)	20 (58.8)	0.245	6 (50)	21 (40)	1.000

Table 6. Comparison of onychoscopic findings with previous studies[4,11-14]

Study	Sample size	Distal irregular termination (%)	Longitudinal striae (%)	Intermittent spiked pattern (%)	Chromonychia (%)	Subungual hyperkeratosis (%)
Jesus-Silva et al.	155	43.23	60.7	25	21.94	-
Maatouk et al.	45 (DLSO)	5-11	31-68	25-55	-	-
Chetana et al.	234	34.6	49.1	43.6	-	-
Kayarkatte et al.	88	81.8	25	86.4	85.2	85.2
Sangeetha et al.	122	23	81.1	80.3	-	-
Our study	52	69.2	59.6	44.2	100	51.9

more frequent in TDO, but with no statistically significant difference. The only patient with PSO presented with brown discoloration, proximal onycholysis, and opacity of the nail plate, jagged proximal edge, intermittent spiked pattern, and distal irregular termination.

When comparing the onychoscopic features of onychomycosis caused by *Candida* with others, there was no remarkable difference in colour (Table 5), but distal irregular termination was significantly lower (50% vs. 79.4%), and a linear edge, observed in 88% of candidal onychomycosis, and subungual hyperkeratosis observed in 38.8% were not significantly different.

Fusarium-affected nails showed more brown discolorations (33.3%), but less nail plate opacity (50% vs.

80%). Jagged proximal edges, distal irregular termination, intermittent spiked pattern, and rough longitudinal white edge were very frequently observed in these affected nails (Table 5).

In three patients with *Trichosporon* infection, all with DLSO, two showed yellow and one green colour, all had longitudinal striae and distal irregular termination, two had opacity and jagged proximal edge, and one had trachyonychia.

Discussion

Our study was carried out in 52 adult patients with onychomycosis within the most common age group (40-50 y), with more females, similar to other reported studies[10,11]. DLSO was the commonest type of clinical presentation in all organisms, namely in *Candida, Fusarium,* and *Trichosporon* infections. The only case of PSO showed Candida on culture, and Candida *spp* was also the most common isolate in TDO.

Comparing onychoscopic features of our studies with previous ones (Table 6)[4,11-14]. We found a previously unreported finding in 46.2% of onychomycosis, a "shallow layered appearance."

In our study, most patients with DLSO presented with yellowish discoloration, distal lateral onycholysis, distal irregular termination, and nail plate opacity (60.5%) but only 55.3% of DLSO showed longitudinal white striae, in contrast to studies done by Jesus-Silva et al. (62.6%), Nargis et al. (100%), (100%), and Yadav et al. (100%)[4,15,16] TDO type presented with total nail onycholysis, distal irregular termination, and subungual hyperkeratosis (81.8%), similar to the study by Chetana et al., but longitudinal white striae were much more frequent in our study (63.3% vs. 10%)[12].

The association between clinical features, onychoscopic findings, and etiology based on nail culture has rarely been studied. In our study, nails with candidal growth in culture showed more common yellow and brown discolouration compared to other organisms, whereas nail plate opacity, intermittent spiked pattern, and linear edge were only slightly more frequent. Compared to the study by Abdallah et al.[6] that found mostly longitudinal white striae (85.7%), spiked pattern (64%), subungual hyperkeratosis (42%), distal irregular termination (57.7%), and jagged proximal edge (64%) in candidal nail infection, our findings are not significantly different.

We cannot compare our results in onychomycosis due to *Fusarium* or due to *Trichosporon* because, as far as we know, there are no published studies on onychoscopic findings in the nail infections by these agents.

Limitations

The small study population is a limitation. The diagnostic accuracy of onychomycosis could have been augmented if histopathological examination and Periodic Acid-Schiff stain were used. The low culture positivity rate and absence of dermatophytes in culture limit the generalization of this study.

Conclusions

Onychoscopy can be used as a non-invasive diagnostic aid in onychomycosis, where investigations such as KOH examination and culture have low sensitivity. Chromonychia and onycholysis are observed on onychoscopy in almost all patients. Shallow-layered appearance is a newly detected onychoscopic feature, whose specificity needs to be evaluated. Distal irregular termination was significantly lower in candidal onychomycosis compared to others. *Fusarium*-affected nails showed more brown discolorations and jagged proximal edges and an intermittent spiked pattern in onychoscopy than others. This study shows an association between onychoscopic features and the causative agents in onychomycosis, but further studies with a substantial use of onychoscopy are necessary for defining the real value of onychoscopy in diagnosing onychomycosis and suggesting its cause, therefore contributing to better orient its treatment.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the World Medical Association and the Declaration of Helsinki. The procedures were authorized by the Institutional Ethics Committee.

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 (AI). 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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ORIGINAL ARTICLE

Unilateral pedicled myocutaneous island flap for nasal tip reconstruction: a case series

Retalho miocutâneo em ilha com pedículo unilateral para reconstrução da ponta nasal: uma série de casos

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Abstract

Objective: To describe the surgical technique, indications, and clinical outcomes of the unilateral pedicled myocutaneous island advancement flap for nasal tip reconstruction following tumor excision. **Methods:** A retrospective observational study was conducted, including nasal tip reconstructions performed between 2024 and 2025 using a unilateral pedicled myocutaneous island advancement flap at the Unidade Local de Saúde de Almada-Seixal. All procedures were performed under local anesthesia. **Results:** Five patients were included (four women and one man; mean age 63.8 years). All lesions corresponded histologically to basal cell carcinoma, and one reconstruction was performed following Mohs micrographic surgery. In all patients, the flap provided adequate mobility to close the defect without excessive tension or tip elevation. No major complications or flap loss occurred. **Conclusion:** The unilateral pedicled myocutaneous island flap is a reliable and versatile technique for nasal tip reconstruction, offering robust vascularity, good tissue conformity, and preservation of nasal contour. Despite its technical demands and potentially visible scar geometry, this flap is a valuable reconstructive choice for selected nasal tip defects.

Keywords: Basal cell carcinoma. Nasal reconstruction. Nasal tip. Myocutaneous island flap.

Resumo

Objetivo: Descrever a técnica cirúrgica, as indicações e os resultados clínicos da utilização do retalho miocutâneo de avanço em ilha com pedículo unilateral na reconstrução da ponta do nariz após excisão tumoral. **Métodos:** Foi realizado um estudo retrospetivo observacional, que incluiu reconstruções da ponta do nariz realizadas entre 2024 e 2025 com recurso ao retalho miocutâneo de avanço em ilha com pedículo unilateral, na Unidade Local de Saúde de Almada-Seixal. Todas as cirurgias foram realizadas sob anestesia local. **Resultados:** Foram incluídos cinco doentes (quatro mulheres e um homem; idade média 63,8 anos). Todas as lesões correspondiam histologicamente a carcinoma basocelular e uma das reconstruções foi realizada após cirurgia micrográfica de Mohs. Em todos os doentes o retalho proporcionou uma mobilidade adequada para encerrar o defeito sem tensão excessiva ou elevação da ponta do nariz. Não ocorreram complicações graves nem necrose do retalho. **Conclusõe:** O retalho miocutâneo em ilha com pedículo unilateral é uma técnica fiável e versátil para a reconstrução

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de defeitos cirúrgicos ponta do nariz, promovendo uma vascularização robusta, boa conformidade tecidular e preservação do contorno nasal. Apesar da sua exigência técnica e da possibilidade de uma configuração cicatricial mais visível, este retalho é uma opção reconstrutiva valiosa para defeitos selecionados da ponta do nariz.

Palavras-chave: Carcinoma basocelular. Reconstrução nasal. Ponta do nariz. Retalho miocutâneo em ilha.

Introduction

Nasal reconstruction after surgical excision carries substantial cosmetic relevance due to the central and highly visible position of the nose on the face[1]. Successful nasal reconstruction requires meticulous attention to color and texture match, contour, and the symmetry of nasal subunits[2]. Island flaps offer excellent color and texture compatibility as well as tissue conformity; however, the limited mobility of the nasal subcutaneous tissue often restricts their use[2]. Among the possible modifications of the island flap, the use of a unilateral myocutaneous pedicle has been described[3]. This unilateral pedicled myocutaneous island flap enhances flap mobility while preserving its reliable vascular supply[4]. Despite previous descriptions in the literature, case series focusing exclusively on unilateral pedicled myocutaneous island flaps for nasal tip reconstruction remain limited.

The surgical technique is described as follows. The procedure begins with identification of the lesion and surgical margins (Fig. 1A). The course of the facial artery and, subsequently, the angular artery can be visualized. Flap vascularization is provided by branches of the angular artery that accompany the fibers of the transverse nasal muscle (*musculus nasilis, pars transversa*).

A triangular flap is then designed superior to the defect, ensuring that the base of the triangle corresponds to the defect diameter, while the flap length should measure approximately 3 times the defect diameter (Fig. 1B). An incision is made around the flap, creating an island configuration (Fig. 1C). Importantly, the incision along the side containing the intended muscular pedicle is limited to the subcutaneous tissue, thereby preserving muscle integrity. On the side opposite the pedicle, a deeper incision is made down to the nasal cartilage or bone, transecting the transverse nasal muscle (Fig. 1D).

Flap elevation is performed in two distinct planes: first, undermining of the lateral nasal wall ipsilateral to the muscular pedicle within the subcutaneous plane up to the nasofacial sulcus; second, undermining of the

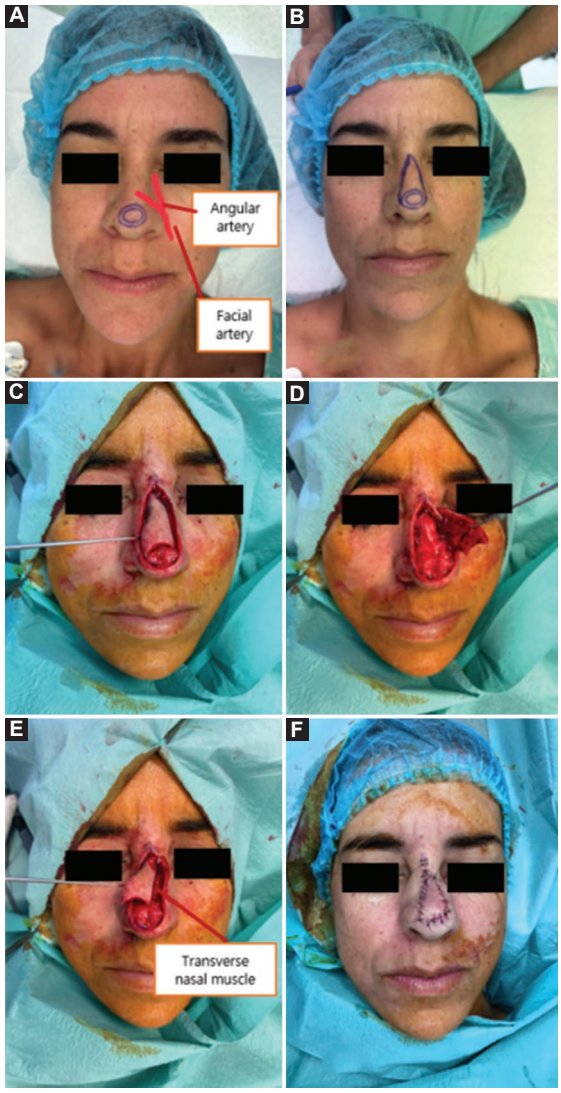

Figure 1. Corresponding to case 1. Surgical steps of the unilateral pedicled myocutaneous island flap for nasal tip reconstruction. **A:** pre-operative marking of the lesion and margins, with the anatomical course of the facial and angular arteries indicated. **B:** design of the triangular skin island superior to the defect. **C:** circumferential incision outlining the Island flap. **D:** creation of the deeper incision on the side opposite the pedicle, extending to cartilage or bone. **E:** identification and preservation of the transverse nasal muscle fibers forming the myocutaneous pedicle. **F:** final result after advancement and V-Y closure.

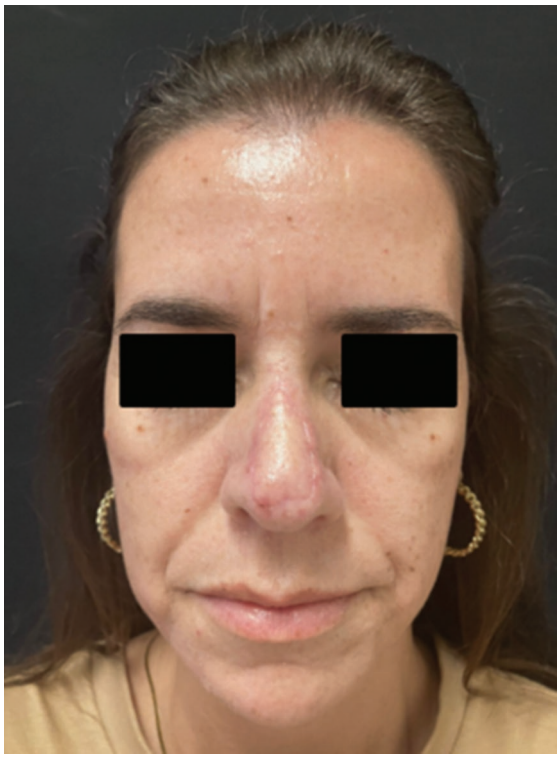

Figure 2. Corresponding to case 1. Post-operative outcome at 1 month.

flap inferior to the transverse nasal muscle along the lateral nasal wall to the nasofacial sulcus.

The flap is then advanced to cover the defect (Fig. 1E), and closure is performed in a V-Y fashion (Fig. 1F).

Methods

This was a retrospective, observational, single-center study including clinical cases of surgical reconstruction of nasal tip defects performed over a 2-year period (2024-2025) at the Unidade Local de Saúde de Almada-Seixal. All reconstructions were carried out using a unilateral pedicled island myocutaneous advancement flap. Procedures were performed under local anesthesia on an outpatient basis, with no need for hospital admission.

Results

A total of five patients were included in this series, comprising four women (80%) and one man (20%). The mean age at the time of surgery was 63.8 years. One of the reconstructions was performed following tumor excision with Mohs micrographic surgery. Histopathological analysis was available for all five cases. In every patient

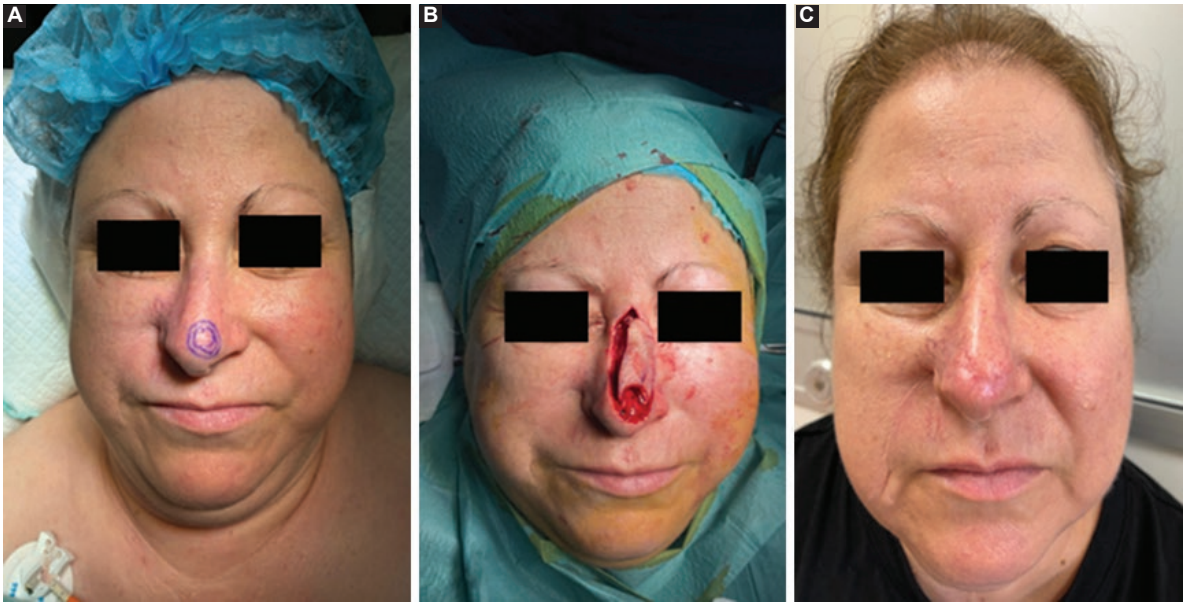

Figure 3. Corresponding to case 2. **A:** pre-operative identification of the lesion and surgical margins. **B:** intraoperative view demonstrating the intermediate stage of flap advancement using the unilateral pedicled myocutaneous island flap. **C:** final esthetic outcome at 2 months postoperatively.

(100%), the excised lesion corresponded to a basal cell carcinoma.

Case 1: A 41-year-old female with a basal cell carcinoma on the nasal tip. This case was used to illustrate the flap design in the introduction (Fig. 1). Primary closure would have generated excessive tension and an undesirable elevation of the nasal tip. An acceptable esthetic outcome was observed at 1 month postoperatively (Fig. 2).

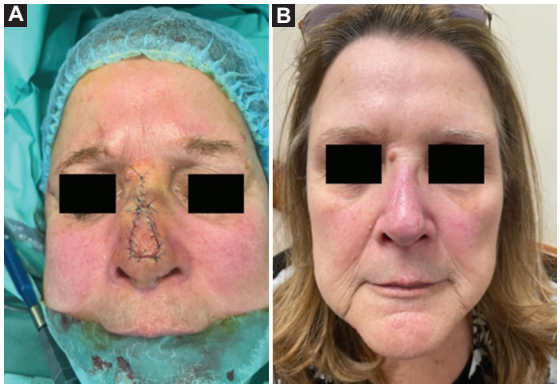

Figure 4. Corresponding to case 3. No pre-operative photograph of the initial lesion is available. **A:** immediate post-operative appearance following reconstruction with a unilateral pedicled myocutaneous island flap. **B:** esthetic outcome at 3 months postoperatively.

Case 2: A 52-year-old female with a basal cell carcinoma on the nasal tip. Reconstruction was performed following Mohs micrographic surgery. A good esthetic outcome was documented at 2 months postoperatively (Fig. 3).

Case 3: A 71-year-old female with a basal cell carcinoma on the nasal tip. A good esthetic outcome was achieved at 3 months postoperatively (Fig. 4).

Case 4: A 75-year-old female with a basal cell carcinoma on the nasal tip. An excellent esthetic outcome was obtained 2 months after surgery (Fig. 5).

Case 5: An 80-year-old male with a basal cell carcinoma on the nasal tip. An acceptable esthetic outcome was noted at 3 months postoperatively (Fig. 6).

Discussion and conclusion

The unilateral pedicled myocutaneous flap is a variant of the island flap with excellent mobility and a reliable vascular supply provided by the angular artery, a branch of the facial artery[1].

Myocutaneous pedicles broaden the indications for island flaps by enabling an alternative source of perfusion. However, their design and elevation are technically demanding[2].

The main advantages of this flap include its robust vascularity, substantial mobility, and excellent color and

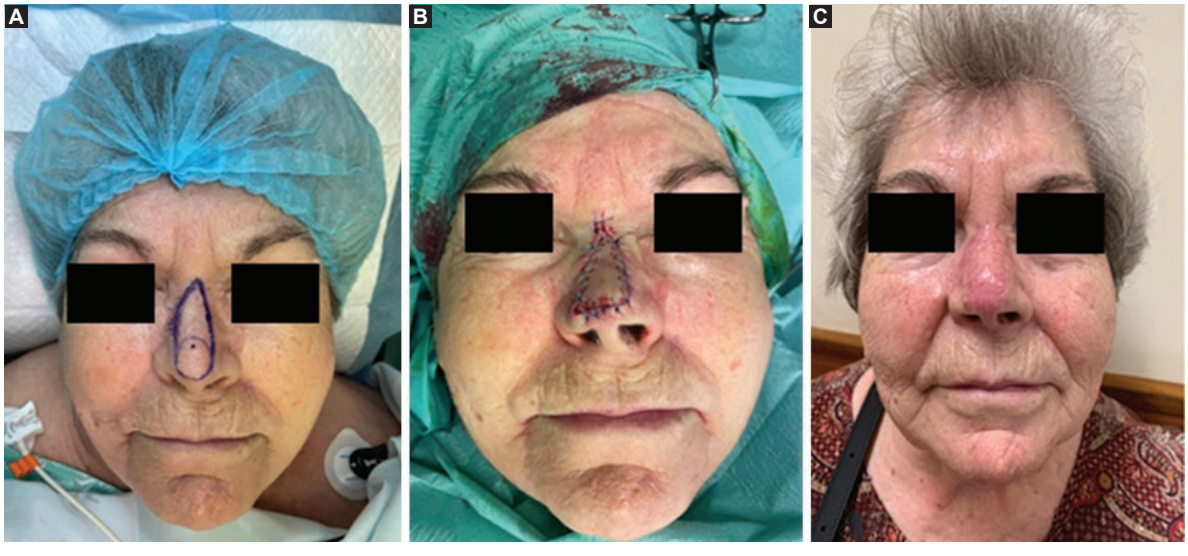

Figure 5. Corresponding to case 4. **A:** pre-operative identification of the surgical margins and flap design. **B:** immediate post-operative appearance following reconstruction with a unilateral pedicled myocutaneous island flap. **C:** excellent esthetic outcome at 2 months postoperatively.

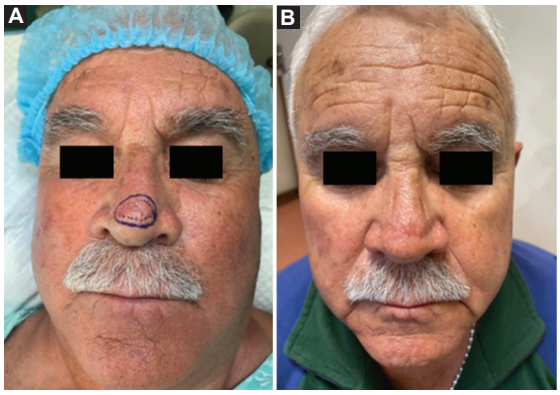

Figure 6. Corresponding to case 5. **A:** pre-operative identification of the lesion and surgical margins. **B:** acceptable esthetic outcome at 3 months postoperatively following reconstruction with a unilateral pedicled myocutaneous island flap.

texture match with the surrounding skin[5], while generally avoiding undesirable elevation of the nasal tip[1].

The main disadvantages relate to its geometric configuration, which may result in a more conspicuous scar.

In this case series, the mean patient age was relatively young (63.8 years), underscoring the need for meticulous attention to reconstructive planning and execution, particularly in esthetic subunits such as the nasal tip. Although the sample size is limited, the consistent post-operative outcomes across all cases support the reliability and versatility of this flap design. Our findings reinforce that this flap is particularly advantageous in younger patients or in those where distortion of the nasal tip must be minimized.

Overall, the unilateral pedicled myocutaneous island flap provides a reliable, safe, and versatile option for reconstruction of distal nasal dorsum and nasal tip defects, particularly when tissue mobility is limited and preservation of nasal contour is essential.

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 (AI). 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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ORIGINAL ARTICLE

Impact of hair loss on quality of life and mental health: a comparative study of androgenetic alopecia and alopecia areata

Impacto da queda de cabelo na qualidade de vida e saúde mental: um estudo comparativo entre alopécia androgenética e alopécia areata

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Abstract

Objectives: Hair has a crucial role in the esthetic appearance of a person, making them look young and confident. Hair loss overall affects self-esteem and is thus prone to psychiatric comorbidities such as depression and anxiety. Thus, this study aims to know the quality of life in patients suffering from common hair loss conditions, such as androgenetic alopecia (AGA) and alopecia areata (AA). **Methods:** A total of 200 AGA and AA patients were enrolled in this study. Dermatology Life Quality Index (DLQI) questionnaire, Beck Depression Inventory Scale (BDI), Beck Anxiety Inventory Scale (BAI), and Patient Health Questionnaire (PHQ) were used to study the quality of life and psychiatric comorbidities in them. **Results**: A total of 88 AA and 112 AGA patients were enrolled in our study. The mean DLQI score was 12.34 in AA and 12.93 in AGA, which implied a large effect on QoL. The mean BAI scale was 22.35 in AA and 22.18 in AGA, and the mean BDI scale was 24.63 in AA and 26.34 in AGA, which implied a moderate effect of anxiety and depression. Almost 50% of patients in AGA showed severe anxiety. PHQ in AA and AGA showed a significant difference in depressive and binge eating disorders. **Conclusions:** There was a large impact on the QoL amongst all of our patients, and anxiety and depression were moderately documented. There was no statistically significant difference between the psychiatric comorbidities among patients with AA and AGA. Understanding the psychological impact on the patients of AA and AGA can help with effective counseling and treatment.

Keywords: Alopecia areata. Androgenic alopecia. Beck anxiety inventory scale. Beck depression inventory scale. Dermatology life quality index.

Resumo

Objetivos: O cabelo desempenha um papel crucial na aparência estética de uma pessoa, fazendo-a parecer jovem e confiante. A queda de cabelo, em geral, afeta a autoestima e, por isso, predispõe-na para comorbilidades psiquiátricas, como a depressão, a ansiedade, etc. Assim, este estudo tem como objetivo avaliar a qualidade de vida em doentes que sofrem de condições comuns de queda de cabelo, como a alopécia androgenética (AAG) e a alopécia areata (AA). **Métodos:** Um total de 200 doentes com AAG e AA foram incluídos neste estudo. O questionário Dermatology Life Quality Index (DLQI), a escala

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Beck Depression Inventory (BDI), a escala Beck Anxiety Inventory (BAI) e o Patient Health Questionnaire (PHQ) foram utilizados para estudar a qualidade de vida e as comorbilidades psiquiátricas. **Resultados:** Um total de 88 doentes com AA e 112 com AAG foram incluídos no nosso estudo. A pontuação média do DLQI foi de 12,34 no AA e de 12,93 no AIG, o que implicou um grande efeito na qualidade de vida. A escala média do BAI foi de 22,35 no AA e de 22,18 no AIG, e a escala média do BDI foi de 24,63 no AA e de 26,34 no AIG, o que implicou um efeito moderado da ansiedade e da depressão. Quase 50% dos doentes em AIG apresentaram ansiedade grave. O PHQ em AA e AIG mostrou uma diferença significativa nas perturbações depressivas e de compulsão alimentar periódica. **Conclusões:** Houve um grande impacto na qualidade de vida entre todos os nossos doentes, e a ansiedade e a depressão foram moderadamente documentadas. Não houve diferença estatisticamente significativa entre as comorbilidades psiquiátricas entre os doentes com AA e AIG. Compreender o impacto psicológico nos doentes com AA e AIG pode auxiliar no aconselhamento eficaz durante o tratamento.

Palavras-chave: Alopecia areata. Alopecia androgenética. Escala de inventário de ansiedade de beck. Escala de inventário de depressão de beck. Índice de qualidade de vida em dermatologia.

Introduction

Alopecia is defined as the loss of hair on the scalp and sometimes on the body as well. As a chronic dermatological condition, it can cause anxiety and/or depression according to various studies[1]. Alopecia can be classified into cicatricial and non-cicatricial alopecia. The main causes of non-cicatricial alopecia are telogen effluvium, androgenetic alopecia (AGA), and alopecia areata (AA)[2]. Among them, AA and AGA are easily visible and can affect the physical appearance of an individual. AGA affects about 50% of men and 19% females, and AA can affect 2.1% of the population[3-5].

Hair loss is perceived in terms of an abnormality because it does not conform to the norms of physical appearance in a society and has the potential to make an individual lose their own self-worth[6]. Therefore, it is critical for physicians to understand how alopecia affects patients' quality of life (QoL) and assess the severity of this impact.

In this study, we aim to assess how the two common non-cicatricial alopecias (AA and AGA) affect the appearance and QoL of these patients, screen for psychiatric comorbidities such as anxiety, depression, and other psychiatric disorders, and compare these effects on the two subtypes of alopecia.

Methodology

We conducted a cross-sectional study on all consenting patients above 18 years suffering from AGA or AA on the scalp, diagnosed clinically and by dermoscopy, who visited the dermatology outpatient department between March and August 2020. We excluded patients suffering from other skin conditions, known psychiatric disorders, or any other chronic diseases that could have an effect on QoL. Furthermore, patients under treatment in the past 6 months were excluded from the study. The sample size was calculated to be 200 according to Fisher's formula.

Ethical committee clearance was obtained from the institutional ethics committee. Informed consent was obtained from patients participating in the study. The demographic details were collected, and a complete history and physical examination were conducted, reporting the type of non-scarring alopecia on the basis of the history and clinical and dermoscopic examination.

The severity of the non-scarring alopecia was assessed by SALT scoring for AA and the Hamilton Norwood scale for androgenic alopecia. Under psychiatric supervision, all patients were explained about the DLQI questionnaire and the Beck Depression Inventory Scale (BDI) and BAI scale. Patients were screened for psychiatric comorbidities such as bulimia, panic syndromes, and somatic disorders using patient health questionnaires (PHQ), a self-report inventory that includes multiple-choice questions for screening and diagnosis of mental health disorders, and the diagnosis was confirmed clinically by a psychiatrist. All patients were offered dermatological and psychiatric treatment when warranted.

Data were analyzed using the Statistical Package for the Social Sciences version 21. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies (%). Quantitative data were compared using the Chi-square test. Pearson simple correlation analyses were performed to determine associations between continuous parameters. A $p < 0.05$ was considered statistically significant.

Results

A total of 200 patients with alopecia were interviewed during the study period. The mean age was 33.92 ±

Table 1. DLQI scores according to the type of alopecia

DLQI score	Characteristic	Alopecia areata (%)	Androgenetic alopecia (%)	p
Mean DLQI score ± SD		12.34 ± 5.43	12.93 ± 7.43	0.534
0-1	No effect	2 (2.3)	8 (7.1)	
2-5	Small effect	12 (13.6)	12 (10.7)	
6-10	Moderate effect	16 (18.2)	22 (19.6)	
11-20	Large effect	52 (59.1)	50 (44.6)	
21-30	Extremely large effect	6 (6.8)	20 (17.9)	

DLQI: dermatology life quality index.

Table 2. BAI scores according to the type of alopecia

BAI score	Characteristic	Alopecia areata (%)	Androgenetic alopecia (%)	p
Mean BAI score ± SD		22.35 ± 11.5	23.2 ± 16.6	0.691
0-7	No effect	8 (9.1)	28 (25)	
8-15	Mild anxiety	20 (22.7)	12 (10.7)	
16-25	Moderate anxiety	26 (29.5)	16 (14.3)	
26-63	Severe anxiety	34 (38.6)	56 (50)	

BAI: beck anxiety inventory.

11.65 years, with a male (58%) and female (42%) ratio of 1.4:1. There were 88 cases (M:58, F:30) of AA and 112 (M:54, F:58) of AGA. The ratio of males-to-females was 1.9:1 and 1:0.9 in AA and AGA, respectively. The mean age was 32.1 ± 10.6 years for AA and 35.4 ± 12.3 years for AGA.

The mean SALT score in AA patients was 2.72 ± 1.14, and the Hamilton–Norwood scale showed stage II (30.35%) and stage III (26.78%) to be more common among AGA patients.

DLQI scores

For the 200 patients with AA and AGA, the DLQI scores ranged from 0 to 30, with a mean score of 12.34 ± 5.43 and 12.93 ± 7.43, respectively. About 59% of AA and 20% of AGA patients had a large impact on QoL, and 6.8% of AA patients had an extremely large impact on QoL as compared to 18% of AGA patients (Table 1).

Beck anxiety and depression inventory scales

Mean BAI score was 22.35 ± 11.5 in AA and 23.2 ± 16.6 in AGA, with moderate anxiety in 29.5% and 14.3%, and severe anxiety in 38.6% and 50 %, respectively, in AA and AGA patients (Table 2).

Mean BDI score was 24.63 ± 12.03 in AA and 26.34 ± 15.5 in AGA. Moderate depression was detected in 38.6% and 25% of AA and AGA patients, and severe to extremely severe depression in 29.6% and 39.3%, respectively (Table 3).

PHQ

Major and other depressive syndromes were significantly higher in AGA (25.89%) compared to AA (10.22%) (p = 0.005). Binge eating disorders were significantly higher (p = 0.025) in AA (27.27%) compared to AGA (8.9%). Other psychiatric disorders were also noted in both AA and AGA (Table 4).

Correlation between DLQI, BAIS, and BDIS with the severity of alopecias

The severity of AA and AGA predominantly showed a very positive correlation to perfect correlation with the DLQI, BAIS, and BDIS scores, indicating that severer the hair loss greater the impact on QoL, anxiety, and depression (Tables 5 and 6).

Table 3. BDI scores according to the type of alopecia

BDI Score	Characteristic	Alopecia areata (%)	Androgenetic alopecia (%)	p
Mean BDI score ± SD		24.63 ± 12.03	26.34 ± 15.5	0.394
1-10	Normal	12 (13.6)	20 (17.9)	
11-16	Mild mood disturbance	12 (13.6)	12 (10.7)	
17-20	Borderline clinical depression	4 (4.5)	8 (7.1)	
21-30	Moderate depression	34 (38.6)	28 (25)	
31-40	Severe depression	16 (18.2)	26 (23.2)	
41-63	Extreme depression	10 (11.4)	18 (16.1)	

BDI: beck depression inventory.

Table 4. Patient health questionnaire according to the type of alopecia

Patient health questionnaire	Alopecia areata (%)	Androgenetic alopecia (%)	p
Q1 Somatic disorder	13 (14.7)	21 (18.75)	0.459
Q2 Major and other depressive syndromes	9 (10.22)	29 (25.89)	0.00512
Q3 Panic syndrome and other anxiety syndromes	21 (23.86)	17 (15.17)	0.12
Q4 Bulimia and anorexia nervosa	13 (14.77)	23 (20.53)	0.29
Q5 Binge eating disorder	24 (27.27)	10 (8.9)	0.0006
Q6 Alcohol abuse	8 (9.0)	12 (10.71)	0.70

Table 5. Correlation between DLQI, BAIS, and BDIS with the severity of AA

AA (n = 88)	Stage	%	Severity	DLQI	r	BAIS	r	BDIS	r
n = 22	S1	1-24	Mild	14.75	+1.00	24.25	+0.99	24.88	+1.00
n = 18	S2	25-49	Moderate	11.5	+0.82	22.25	+0.99	27.96	+1.00
n = 16	S3	50-74	Severe	10.9	+0.96	20.28	+0.93	23.18	+0.99
n = 29	S4	75-99	Very severe	12.2	+0.94	21.64	+1.00	24.04	+0.99
n = 3	S5	100	Alopecia totalis	15.2	+1.00	36.04	+1.00	31.11	+1.00

r: Pearson correlation, + 1.0: perfect positive correlation, +0.90-+0.99: very strong positive correlation, +0.70-+0.89: strong positive correlation.
DLQI: dermatology life quality index; BAIS: beck anxiety inventory scale; BDIS: beck depression inventory scale; AA: alopecia areata.

Discussion

This study included a total of 200 patients, mostly males (58%), and the majority were in the 21-30 years age group (46%), which is typical for these chronic forms of alopecia.

The mean DLQI score was 12.34 and 12.93 in AA and AGA, respectively, which indicated a large effect on QoL in both groups, but superior to the study by Williamson et al., where the score was 8.3[1], and Zhang and Zhang[7] with a score of 6.3. Considering only AA, the mean total DLQI score was 7.9 ± 7.6 and 6.4 ± 5.5, respectively, in the studies by Abedini et al. and Ghajarzadeh et al.[8,9].

From our study, we could interpret that both AA and AGA significantly impacted the QoL, with no statistically significant difference in the mean scores between the two groups. The difference was that almost all AA had a significant impact on QoL, whereas it is noted that the majority of AA patients had a large effect, and in AGA patients, there was a wider distribution, including a higher percentage showing either no effect or an extremely large effect. Embarrassment (60% and 39% in AA and AGA), effect on their social activities (64%

Table 6. Correlation between DLQI, BAIS, and BDIS with the severity of AGA

AGA (n = 112)	Hamilton-Norwood scale (M: 54)	DLQI	r	BAIS	r	BDIS	r
n = 22	Stage I-II Mild	11.06	+ 0.93	30.26	+ 0.96	23.02	+ 0.92
n = 26	Stage III-V Moderate	11.39	+ 0.89	31.96	+ 0.96	24.67	+ 0.90
n = 6	Stage VI-VII Severe	11.72	+ 1.00	33.37	+ 1.00	26.34	+ 1.00
	Ludwig scale (F: 58)						
n = 35	Stage I Mild	13.23	+ 0.90	14.22	+ 0.94	26.33	+ 0.99
n = 16	Stage II Moderate	13.66	+ 0.92	13.11	+ 0.88	28.26	+ 1.00
n = 7	Stage III Severe	16.52	+ 1.00	16.28	+ 1.00	29.42	+ 1.00

r: Pearson correlation, +1.0: perfect positive correlation, + 0.90-+ 0.99: very strong positive correlation, + 0.70-+ 0.89: strong positive correlation.
AGA: androgenetic alopecia; DLQI: dermatology life quality index, BAIS: beck anxiety inventory scale; BDIS: beck depression inventory scale.

and 41% in AA and AGA), and uncomfortable treatment (49% and 41% in AA and AGA) were some of the contributing factors for the decrease in QoL in our study.

In our study, the prevalence of severe anxiety was 38.6% and 50%, with mean anxiety scores of 22.35 ± 11.5 and 23.2 ± 16.6 in AA and AGA patients, respectively. AGA patients were significantly ($p < 0.05$) more prone to severe anxiety compared to AA. Psychiatric disorders and AA might share some pathophysiologic mechanisms, and there are theories that stress neuroendocrine immunology might play an important role[10]. Trembling of hands (42% in AA and 34% in AGA), difficulty in breathing (49% in AA and 23% in AGA), feeling hot and wobbly, unable to relax, unsteadiness, and heart pounding were reported in an average of 42-51% among both AA and AGA. In our study, 25% of AGA, as compared to 9.1% in AA, showed no anxiety symptoms, which is a significant difference between the two groups ($p < 0.001$), but a greater proportion of AGA patients (50%) fall into the severe anxiety category, compared to 38.6% of AA patients. AGA patients are more likely to either have no anxiety or severe anxiety – suggesting a potential bimodal distribution in emotional response. This could point to differing psychological impacts of visible versus progressive hair loss types. A systematic review by Villasante Fricke and Miteva reported that there was a lifetime prevalence of 66-74% of psychiatric disorders, a 39-62% prevalence of depression, and a 39-62% prevalence of generalized anxiety disorder. Furthermore, QoL was reported to be decreased in half of the AA patients[11].

The prevalence of severe depression among AA patients (11.4%, with mean score 24.63 ± 12.03) is comparable with another study where 65.9% of persons with AA had depression or anxiety[10] and contrasts with Karia et al. study that reported relatively low levels of anxiety (4%) and depression (18%) in AA patients[12] and Vélez-Muñiz et al. study that, using the same assessment tools (BDI and BAI) found no difference in the levels of depression and anxiety between AA and controls[13]. There is growing evidence that depression could be before the onset of AA[14].

Depression was similar in AGA patients (16.1% with a mean score of 26.34 ± 15.5), but AGA patients skewed more toward severe and extreme depression, whereas AA patients had more in the moderate range. Discouraged about the future (58% in AA and 48% in AGA), irritated or annoyed (47% in AA and 45% in AGA), worried about physical problems (47% in AA and 41% in AGA) are some of the depressive symptoms noted in our study.

Overall, both groups show high rates of clinical depression, which highlights the psychological burden of hair loss and supports the need for mental health screening in both patient populations, but especially in those with AGA. Interestingly, we observed no statistically significant difference in anxiety or depression scores between AA and AGA groups based on p-values, but AGA patients seem to be associated with more severe cases of both anxiety and depression, whereas AA patients show more moderate levels, indicating potentially more chronic, but less extreme, psychological impact. The strong positive correlation of the severity of alopecia with DLQI, BAIS, and BDIS indicates that even a small visible patch of hair loss can affect the psychiatric well-being of a person.

Using the PHQ, even though we noticed higher incidence of panic syndrome and other anxiety syndromes (23.86%) in AA, significant difference was seen in major and other depressive syndromes in AGA (10.22%)

as compared to AA (25.89%) (p = 0.005) with Binge eating disorders occurring significantly more in AA (27.7%) (p = 0.0006) than in AGA (8.9%). In accordance with our data, in a review by Cash, 52% of women rated their emotional stress for AGA as very to extremely upsetting and also reported negative body image, poorer self-esteem, and social anxiety[15].

Conclusion

There was a large impact on the QoL among AGA and AA patients, and anxiety and depression were moderately documented, with no statistically significant difference between the groups in which concerns psychiatric comorbidities. There is a paucity in research exploring the patient's belief on AA and AGA and how it relates to their mental health. Hence, this study sheds light on the psychosocial effects of the disease. A proper awareness and consciousness about the psychiatric comorbidities associated with this disease is essential for the desirable management of these patients.

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 (AI). 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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CASE REPORT

Eccrine spiradenoma: three case reports

Espiroadenoma écrino: três casos clínicos

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Abstract

Eccrine spiradenoma is a rare benign adnexal tumor, usually presenting as a painful solitary cutaneous nodule. We report three histologically confirmed cases in male patients aged 38 to 62 years, with lesions located on the right arm, forearm, and anterior hemithorax. Only one patient reported pain, underscoring the variability of clinical symptoms. All tumors exhibited the classic biphasic cell population and basement membrane material, without atypia or mitotic activity. Case 1 also demonstrated lymphoid infiltrates and vascular ectasias, with EMA-positive neoplastic epithelial cells. This series highlights uncommon demographic and anatomical presentations and reinforces the importance of histopathological evaluation for accurate diagnosis of eccrine spiradenoma, particularly in atypical settings.

Keywords: Eccrine spiradenoma. Adnexal tumor. Skin nodule. Histopathology.

Resumo

O espiroadenoma écrino é um tumor anexial benigno raro, que habitualmente se apresenta como um nódulo cutâneo solitário e doloroso. Descrevemos três casos histologicamente confirmados em homens entre os 38 e os 62 anos, com lesões no braço, antebraço e hemitórax anterior direitos. Apenas um dos doentes referiu dor, evidenciando a variabilidade clínica. Todos os tumores apresentavam a clássica população celular bifásica e material de membrana basal, sem atipia nem mitoses. O Caso 1 mostrou, ainda, infiltrado linfocitário e ectasias vasculares, com expressão de EMA nas células epiteliais neoplásicas. Esta série salienta apresentações demográficas e anatómicas invulgares, reforçando a importância da avaliação histopatológica no diagnóstico preciso de espiroadenomas écrinos, sobretudo em contextos atípicos.

Palavras-chave: Espiroadenoma écrino. Tumor anexial. Nódulo cutâneo. Histopatologia.

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Introduction

Eccrine spiradenoma is a rare benign adnexal tumor first described in 1956 by Kersting and Helwig as a dermal tumor with sweat gland differentiation[1]. Recent immunohistochemical studies using follicular stem cell markers (e.g., CD200) have suggested a possible origin in the hair follicle bulge, placing it closer to the follicu-losebaceous-apocrine unit[2].

Spiradenomas usually occur in patients between 15 and 35 years old, and there is no racial or sexual predilection for them[3]. They typically present as strikingly painful small solitary nodules on the head, neck, and trunk that can grow to several centimeters, often with a blue, gray, or purple hue[3,4].

Spiradenomas appear to be caused by a defective tumor suppressor gene[5]. While a mutation in the *CYLD* gene on chromosome 16 is found in Brooke-Spiegler syndrome, which features multiple spiradenomas, the specific cause of solitary spiradenomas is not clear[5].

Although benign spiradenomas are rare, malignant transformation is even rarer and occurs almost exclusively in patients older than the age of 50 years[6,7].

This three-case series provides illustrative examples of the histological diversity and diagnostic complexity of eccrine spiradenomas.

Case report

Case 1

A 62-year-old male patient with an unremarkable previous medical history sought treatment for a painless lesion on the right arm that he had for, at least, 2 years. On examination, a 1.5 × 1.3 cm erythematous and nodular lesion was found. Figures 1 A and B illustrates the histopathological findings.

Case 2

A 38-year-old male patient with no previous medical history sought treatment for a painless lesion in the lower anterior right hemithorax that he had for many years. On examination, a 0.9 × 0.7 cm nodular lesion was found. Figures 2 A-C illustrates the histopathological findings.

Case 3

A 58-year-old male patient with no previous medical history sought treatment for a painful lesion on the right forearm that he had for 1 year. On examination, a 1.0 × 0.9 cm superficial and mobile nodule was found. Figures 3 A-D illustrates the histopathological findings.

Histological description

Histological examination of all three cases revealed a well-defined, encapsulated neoplasm located in the dermis and extending into the subcutaneous tissue. The tumors exhibited a dual cell population, with centrally located large, pale cells containing moderate cytoplasm and vesicular nuclei, and peripheral small, basaloid cells with scant cytoplasm and hyperchromatic nuclei. The lobules were surrounded by basement membrane-like material, which was PAS positive. The stroma was vascularized and populated by numerous lymphocytes, with vascular ectasias also noted in some cases. No cytological atypia, mitosis, or necrosis was observed in any of the lesions. Surgical margins were free of tumor in all cases. In addition, in Case 1, lymphoid inflammatory infiltrates and vascular ectasias and EMA expression in neoplastic epithelial cells were also described.

Discussion

The three cases presented highlight both the similarities and variations in the clinical presentation, histopathological findings, and diagnostic considerations of eccrine spiradenomas.

Although typically reported in younger patients, without sexual predilection, this series highlights eccrine spiradenomas in older males (38-62 years), suggesting either a skewed demographic or an underreported trend.

The location of the tumors in these cases varied, with two cases presenting in the upper limbs (right arm and right forearm) and one on the right hemithorax. This is consistent with the literature indicating a predilection for the ventral surface of the upper half of the body[8].

The main clinical feature, present in about 91% of the patients, is the presence of paroxysmal pain or sensitivity[1]. However, only one of the three patients (Case 3) reported pain. The absence of pain in the other two cases highlights the variability of symptomatology, even in tumors classically described as painful.

In all cases, the lesions were initially suspected to be other cutaneous conditions – such as hemangioma, epidermoid cyst, lipoma, dermatofibroma, neurofibroma, leiomyoma, schwannoma, and nodular basal cell carcinoma – underscoring the clinical challenge of diagnosing eccrine spiradenomas based on clinical features alone. Notably, several of these entities also fall within the differential diagnosis of painful skin tumors, often remembered through the mnemonic “LEND AN EGG,” which includes leiomyoma, eccrine spiradenoma, neuroma, dermatofibroma, angiolipoma, neurilemmoma, endometrioma,

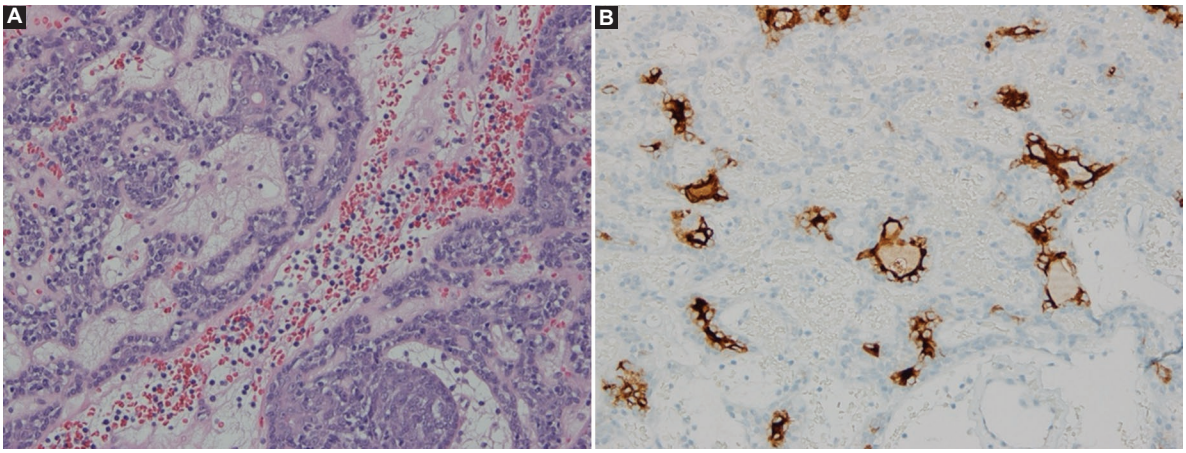

Figure 1. Histopathological findings. **A:** tumor composed of nests and cords of cells surrounded by basement membrane material and composed of two types of cells (clear and dark cells) with some ductal structures (H&E, ×200); **B:** luminal cells of ductal structures with immunoreactivity for EMA (EMA, ×400).

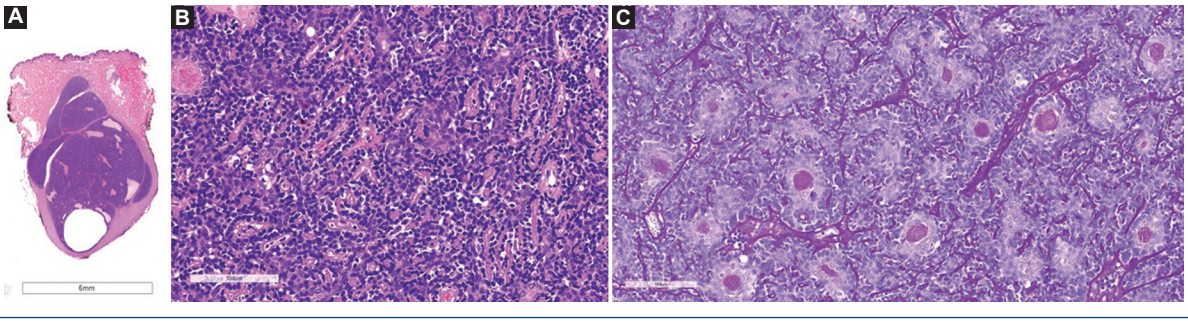

Figure 2. Histopathological findings. **A:** dermis and hypodermis exhibit a well-circumscribed nodular basophilic tumor with cystic changes (H&E, low magnification); **B:** tumor is composed of dual cell population arranged in trabecular fashion with tubular structures (H&E, ×200); **C:** PAS stains basement membrane material within the tubules (PAS, ×200).

glomus tumor, and granular cell tumor[9]. This further reinforces the necessity of histopathological examination for accurate diagnosis, which remains the gold standard.

Although most spiradenomas are sporadic and solitary, a subset may arise in the context of Brooke-Spiegler syndrome (also known as CYLD cutaneous syndrome), an autosomal-dominant disorder characterized by multiple benign adnexal tumors, most commonly spiradenomas, cylindromas, and trichoepitheliomas that typically manifest during childhood or early adolescence[10-12]. None of the patients had a personal history of excision of other benign cutaneous tumors nor any family history suggestive of Brooke-Spiegler syndrome. On physical examination, the tumors appeared to be isolated lesions without other adnexal tumors, and none had arisen during childhood or adolescence. In addition, during a one-year follow-up period, no new benign skin tumors were identified. Therefore, although clinical genetic testing for a germline CYLD pathogenic variant should be considered in individuals with two or more biopsy-confirmed cylindromas, spiradenomas, or trichoepitheliomas, alone or in combination, such testing was not deemed necessary in these cases.

Conclusion

This series of three cases reinforces the clinical and histopathological diversity of eccrine spiradenomas, while also challenging conventional assumptions regarding their demographic and anatomical distribution. The presentation in older male patients, with predominantly painless lesions and locations on the ventral upper body, highlights the need to consider this diagnosis even in atypical contexts. The histological findings further

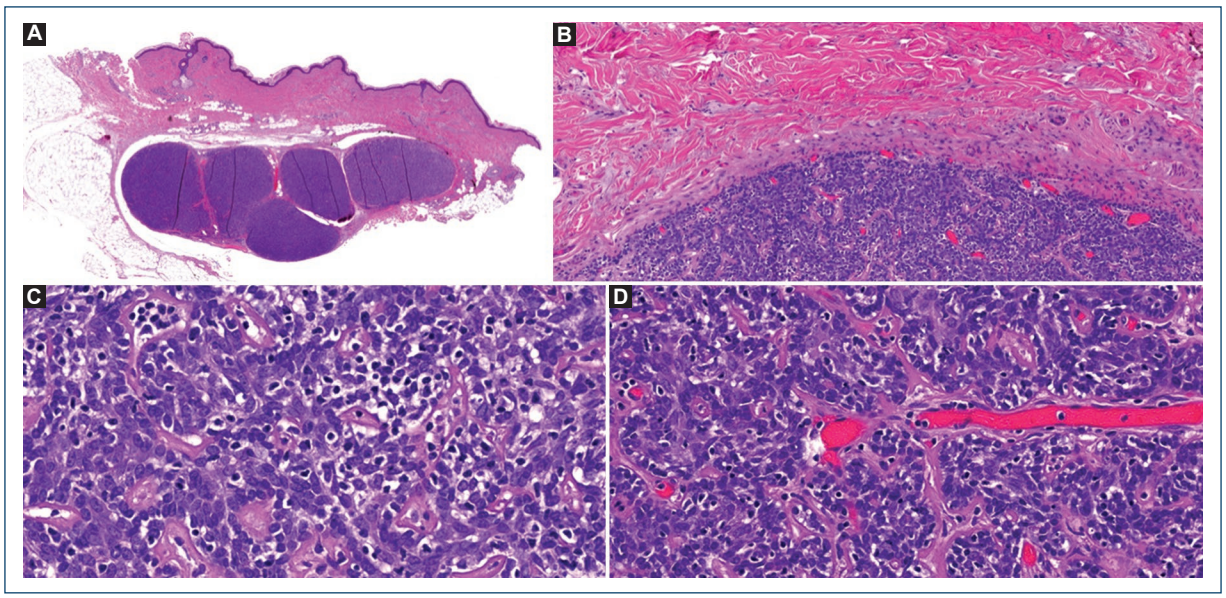

Figure 3. Histopathological findings. **A:** well-circumscribed, basophilic tumor lobules in the dermis and subcutaneous tissue (H&E, low magnification); **B:** the tumor lobules are well marginated and encapsulated by a thin fibrous capsule (H&E, ×100); **C:** the tumor is composed of a biphasic population of smaller basaloid cells and larger clear cells. There is no cytologic atypia, mitosis, or necrosis (H&E, ×200); **D:** vascular stroma with capillary ectasias, basement membrane material, and scattered lymphocytes (H&E, ×200).

illustrate the spectrum of morphological variability. Moreover, the absence of features suggestive of CYLD cutaneous syndrome emphasizes the importance of clinical evaluation in determining the need for genetic testing. Ultimately, this series underscores the diagnostic value of histopathology in distinguishing eccrine spiradenomas from other painful or indolent subcutaneous tumors.

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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 obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence (AI). 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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CASE REPORT

Multiple arcuate lesions over neck of an adult: a case of atypical elastosis perforans serpiginosa

Múltiplas lesões em arco no pescoço de um adulto: um caso atípico de elastose perfurante serpiginosa

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Abstract

Elastosis perforans serpiginosa (EPS) is a rare disorder of the skin, usually present in early adulthood over the neck, upper arms, or face, associated with various genetic, cardiac, and renal comorbidities. A 38-year-old male presented with multiple painless, intensely itchy lesions over the neck for 6 months with insidious onset and gradually progressive number. There was no significant drug history or family history, or associated comorbidities or history of any intellectual disability. On examination, multiple non-tender arcuate plaques were present over the nape of the neck, without any scaling or ulceration. Due to a diagnostic dilemma, a biopsy was done, which showed elongated rete ridges forming a channel containing basophilic debris with numerous thick twisted wavy fibers with lymphocytic infiltrates. Verhoeff-Van Gieson staining came positive for elastic fibers. Hence, the case was diagnosed as idiopathic elastosis perforance serpiginosa. Lesions resolved after application of 0.05% tretinoin cream for 3 months. EPS is an uncommon disease of childhood or early adulthood, usually asymptomatic and associated with various genetic, cardiac, or renal comorbidities or drug intake. But here, lesions appeared at late adulthood, were intensely pruritic with no associated factors. Hence, the case was atypical in terms of onset, symptoms, and causal association; hence presented here.

Keywords: Elastosis perforans serpiginosa. Arcuate. Elastin. Verhoeff-Van Gieson. Basophilic debris.

Resumo

A elastose perfurante serpiginosa é uma doença rara da pele que geralmente se manifesta no início da idade adulta, afetando o pescoço, os braços superiores ou o rosto, e está associada a várias comorbidades genéticas, cardíacas e renais. Um homem de 38 anos apresentou múltiplas lesões indolores e intensamente pruriginosas no pescoço há seis meses, de início insidioso e número progressivamente crescente. Não havia histórico significativo de uso de medicamentos, antecedentes familiares, comorbidades associadas ou deficiência intelectual. Ao exame físico, observaram-se múltiplas placas arqueadas não dolorosas na nuca, sem descamação ou ulceração. Devido ao dilema diagnóstico, foi realizada biópsia que revelou cristas epidérmicas alongadas formando um canal contendo detritos basofílicos, com numerosas fibras espessas, torcidas e onduladas, além de infiltrado linfocitário. A coloração de Verhoeff-Van Gieson foi positiva para fibras elásticas. Assim, o caso foi diagnosticado como elastose perfurante serpiginosa idiopática. As lesões regrediram após aplicação de creme de tretinoína a 0,05% por três meses. A elastose perfurante serpiginosa é uma doença incomum da infância ou início da idade adulta,

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geralmente assintomática e associada a diversas comorbidades genéticas, cardíacas, renais ou ao uso de medicamentos. No entanto, neste caso, as lesões surgiram tardiamente na idade adulta, eram intensamente pruriginosas e sem fatores associados, configurando, portanto, uma apresentação atípica quanto ao início, sintomas e causa.

Palavras-chave: Elastose perfurante serpiginosa. Arqueado. Elastina. Verhoeff-Van Gieson. Detritos basofílicos.

Introduction

Elastosis perforans serpiginosa (EPS) is a rare perforating dermatosis characterized by transepidermal elimination of altered elastic fibers from the dermis[1]. It belongs to the primary perforating disorders, where degenerated elastic tissue is extruded through epidermal channels, forming distinctive lesions[2]. EPS typically presents in childhood or early adulthood with a male predominance and an estimated prevalence of < 1 in 100,000[3]. Clinically, it manifests as asymptomatic, hyperkeratotic papules arranged in arcuate, serpiginous, or annular patterns, commonly on the neck, face, or upper extremities[4]. Lesions are often self-limiting but may persist or recur.

EPS is classified into idiopathic (50-70% of cases), reactive (associated with connective tissue disorders such as pseudoxanthoma elasticum, Ehlers–Danlos syndrome, or Down syndrome), and drug-induced (commonly linked to long-term penicillamine therapy)[5-7].

Associated comorbidities include cardiovascular anomalies, renal diseases, or intellectual disabilities in syndromic cases[8]. Histopathologically, EPS shows acanthosis, hyperkeratosis, and transepidermal channels containing basophilic debris and fragmented elastic fibers, confirmed by Verhoeff-van Gieson (VVG) staining[9]. The etiology involves altered elastin metabolism, possibly due to genetic mutations or external triggers affecting dermal fibroblasts[3]. Diagnosis is clinicopathologic, as clinical mimics include granuloma annulare, porokeratosis, or reactive perforating collagenosis[10]. Treatment is challenging, with topical retinoids, cryotherapy, or laser ablation used anecdotally[11,12]. This case report describes an atypical presentation of idiopathic EPS in a middle-aged adult, highlighting diagnostic challenges and therapeutic success.

Case report

A 38-year-old male presented to the dermatology outpatient department with multiple solid lesions on the neck for 6 months. The lesions were insidious in onset, gradually increasing in number, painless but intensely pruritic, impacting daily activities. He denied preceding trauma, drug intake (including penicillamine), family history of similar lesions, or systemic symptoms such as joint pains or cardiovascular issues. No comorbidities, including connective tissue disorders or genetic syndromes, were reported. Examination revealed multiple non-tender, arcuate plaques bilaterally over the nape of the neck, surrounded by 2-3 mm keratotic papules in a serpiginous pattern, without scaling, ulceration, or erythema (Figs. 1 A and B). No lesions were noted elsewhere. Differential diagnoses included granuloma annulare, annular elastolytic giant cell granuloma, and porokeratosis, but the morphology suggested a perforating disorder.

Laboratory investigations, including complete blood count and renal function tests, were normal. A punch biopsy from a lesion showed irregular acanthosis with elongated rete ridges forming narrow channels containing basophilic debris and thick, twisted elastic fibers (Fig. 1C). The dermis had mild lymphocytic and plasma cell infiltrates (Fig. 1D). Hematoxylin and eosin staining confirmed these findings, and VVG staining highlighted fragmented elastic fibers within the channels, consistent with EPS[9]. No collagen perforation or foreign material was seen. Idiopathic EPS was diagnosed based on clinical and histopathological correlation.

Topical 0.05% tretinoin cream was applied nightly. Pruritus improved within 2 weeks, and lesions resolved completely after 3 months, with no scarring or recurrence at 6-month follow-up.

Discussion

This case is atypical due to its late onset, intense pruritus, and idiopathic nature without associated factors. EPS typically presents before the age of 20 years, with only 15% of cases occurring after 30, often in reactive or drug-induced forms[3]. A systematic review of 68 EPS cases noted late-onset cases are rare and usually linked to comorbidities[3]. The intense pruritus here contrasts with the typically asymptomatic or mildly itchy EPS; pruritus is more common in acquired perforating dermatoses such as those associated with

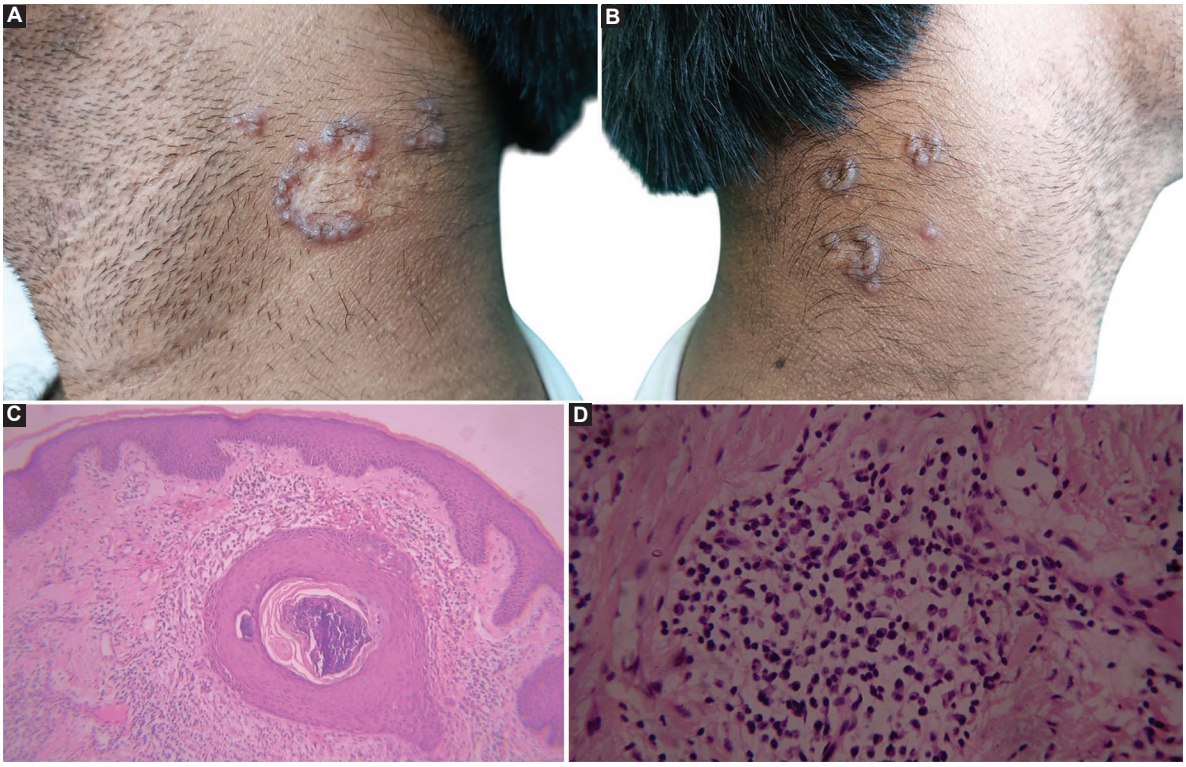

Figure 1. Clinical and histopathological images. **A** and **B:** multiple arcuate plaques bilaterally over the nape of the neck, surrounded by 2-3 mm keratotic papules in a serpiginous pattern. **C:** ×10 magnification showing acanthosis, hyperkeratosis and transepidermal channels containing basophilic debris and fragmented elastic fibers. **D:** ×40 magnification showing mild lymphocytic and plasma cell infiltrates in dermis.

diabetes or renal failure, absent in this patient[2,4]. The dermal lymphocytic and plasma cell infiltrates suggest a heightened inflammatory response, though not typical for EPS[9].

The absence of genetic, drug-related, or systemic associations marks this as a rare idiopathic variant. Approximately 25-40% of EPS cases relate to genetic disorders such as Down syndrome, where elastin synthesis may be disrupted[8,13]. Drug-induced EPS, comprising 20-30% of cases, is strongly associated with penicillamine, which alters elastin cross-linking[5,6,14]. Reactive EPS may occur with pseudoxanthoma elasticum or scabies, triggering elastic fiber degradation[7,10]. This patient's lack of such factors suggests a sporadic elastin gene mutation or unidentified environmental trigger[5].

Histopathology was crucial, showing classic EPS features: transepidermal channels with elastic debris, confirmed by VVG staining[9]. This distinguishes EPS from reactive perforating collagenosis, which involves collagen[2]. Topical tretinoin led to complete resolution, consistent with its role in promoting epidermal turnover and elastic fiber clearance[11,12]. Alternatives such as cryotherapy or CO_2 laser are less effective, and systemic isotretinoin is reserved for refractory cases[4,11]. In drug-induced EPS, discontinuing the offending agent is critical, though lesions may persist[6]. Rare paraneoplastic associations with malignancies like multiple myeloma necessitate systemic evaluation in atypical adult-onset cases[7].

This case underscores the diagnostic challenge of atypical EPS, where biopsy is essential. Future research should explore genetic profiling to clarify idiopathic cases and optimize therapies.

Conclusion

This late-onset, pruritic, idiopathic EPS case without comorbidities highlights the variability of this rare dermatosis. Histopathologic confirmation and topical tretinoin therapy led to resolution, emphasizing conservative management. Clinicians should consider EPS in adults with serpiginous neck lesions, even without classical associations, to avoid misdiagnosis. This report adds to the literature on atypical EPS, advocating for increased awareness in dermatologic practice.

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Conflicts of interest

None.

Ethical considerations

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

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

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

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CASE REPORT

Desmoplastic trichoepithelioma on the face mimicking basal cell carcinoma: a case report and literature review

Tricoepitelioma desmoplásico na face simulando carcinoma basocelular: um relato de caso e revisão da literatura

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Abstract

Desmoplastic trichoepithelioma is a rare benign cutaneous neoplasm that differentiates toward germinative cells of the hair follicle. It can be classified as familial multiple trichoepithelioma, solitary, and desmoplastic, the latter being a rare variant with low incidence and clinical features resembling basal cell carcinoma. We report the case of a 54-year-old female patient who presented with a brownish plaque exhibiting areas of dark pigmentation, an irregular outline, a pearly sheen, and surface telangiectasias in the right paranasal region. Complementary studies, including histopathological and immunohistochemical analyses, were performed to establish the definitive diagnosis. Furthermore, this cutaneous lesion displays both clinical and histopathological characteristics that complicate differentiation between benign and malignant tumors, making immunohistochemistry essential to confirm the desmoplastic variant of trichoepithelioma.

Keywords: Desmoplastic trichoepithelioma. Differential diagnosis. Basal cell carcinoma.

Resumo

O tricoepitelioma desmoplásico é uma rara neoplasia benigna de pele que se diferencia em células germinativas do folículo piloso, e pode ser classificado entre tricoepitelioma múltiplo familial, solitário e desmoplásico, sendo esse último uma variante rara com pouca incidência na população e com similaridades clínicas do carcinoma basocelular. O caso é de uma paciente de 54 anos,que apresentou uma placa acastanhada, com algumas áreas de pigmentos enegrecidos, irregular, com brilho perláceo e telangiectasias em sua superfície na região paranasal direita, sendo realizado exames complementares como o anatopatológico e imunohistoquímico para confirmação completa do diagnóstico. Além disso, essa lesão no tegumento manifesta estruturas tanto clínicas quanto histopatológicas que dificultam na diferenciação de tumores malignos ou benignos, sendo fundamental a realização da imunohistoquímica para confirmar essa variante desmoplásica do tricoepitelioma.

Palavras-chave: Tricoepitelioma desmoplásico. Diagnóstico diferencial. Carcinoma basocelular.

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Introduction

Desmoplastic trichoepithelioma (DT) is a rare benign skin neoplasm of the hair follicle, a variant of trichoblastoma originating from the proliferation of mesenchymal cells[1-3]. The classification of this cutaneous neoplasm can be divided into three forms: familial multiple trichoepithelioma, solitary, and desmoplastic, with the desmoplastic form characterized by increased fibroplasia in the dermis and this tumor should be considered a differential diagnosis for basal cell carcinoma (BCC)[1-3].

In addition, DT shows a predilection for females, particularly young or middle-aged women[4,5]. Its most common manifestations occur on the facial skin as pink or skin-colored papules and nodules that progressively increase in size, often easily confused with the clinical aspects of BCC[4,5]. The histopathology of this neoplasm consists of a histological triad of thin cords of basaloid cells, keratin cysts, and desmoplastic stroma, which are important for both histological differential diagnoses and clinical differentiation from BCC[3-7].

Case report

A 54-year-old female patient was referred for a dermatological consultation due to a facial lesion that had been present for approximately 2 years, showing progressive growth over time without associated symptoms (Fig. 1).

On dermatological examination, a brownish plaque with some black-pigmented areas, irregular shape, pearly shine, and telangiectasias on its surface was observed, measuring 1 cm in the right paranasal region (Fig. 2).

The patient underwent an incisional biopsy of the lesion, followed by histopathological examination, which showed atrophic epidermis and dermis with diffuse proliferation of small nodular masses and cords of basaloid cells with peripheral palisading, including occasional horn cysts, embedded in desmoplastic and myxoid stroma. Bulb-papilla images suggested follicular differentiation (Fig. 3).

The histopathological examination revealed an intradermal epithelial neoplasm, raising differential diagnoses of DT, micronodular BCC, and microcystic adnexal neoplasm. An additional immunohistochemical study confirmed the diagnosis of DT (Table 1).

Following the DT diagnosis, clinical follow-up of the patient was chosen.

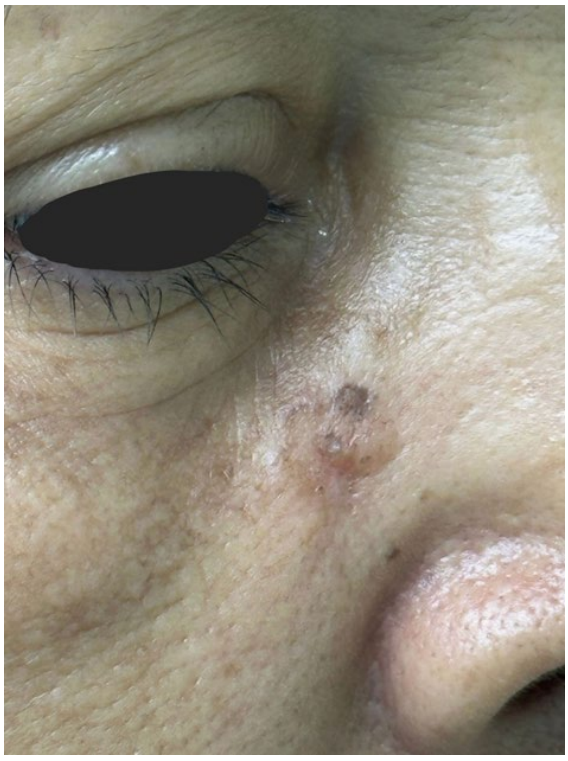

Figure 1. Clinical appearance of the neoplasm.

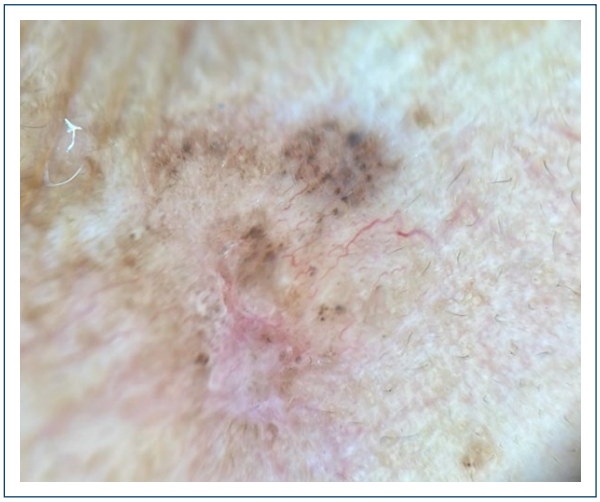

Figure 2. Dermatoscopy of the lesion with irregularly distributed black pigment, tortuous vessels, and mild erythema, measuring 1 cm.

Discussion

BCC is the most common skin neoplasm among non-melanoma skin cancers. Histopathological classification divides BCC into types such as nodular, superficial, and infiltrative. Despite its rare metastatic potential, BCC significantly impacts patient morbidity[1-3]. DT is a

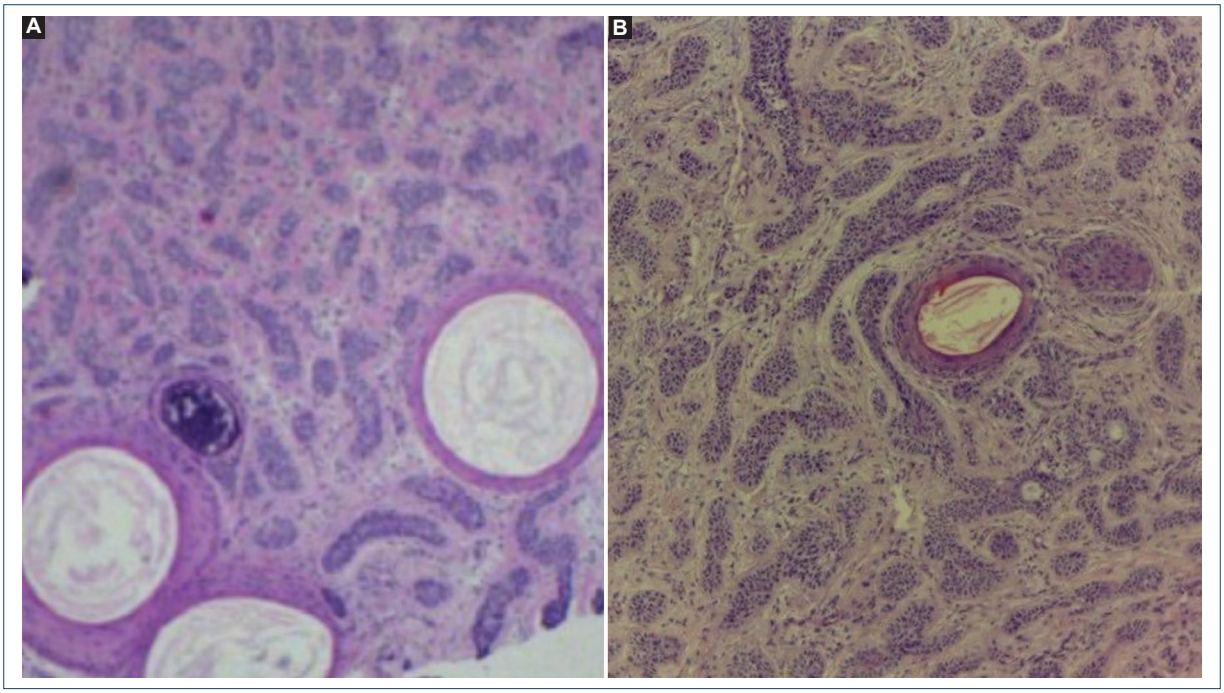

Figure 3. Histopathological findings. **A** and **B:** histological sections, horn cysts, embedded in desmoplastic and myxoid stroma (H&E, x40).

Table 1. Results of the immunohistochemical panel

Antibody	Clone	Result	Observation
Ki-67 (cell proliferation antigen)	MIB1	Positive	5%
p63 protein (squamous/ transitional epithelia; myoepithelial cells)	DAK-p63	Positive	-
Epithelial tumor glycoprotein	BerEp4	Positive	-
Epithelial membrane antigen	E29	Negative	-
Anti-apoptotic protein BCL-2	124	Negative	-

benign cutaneous tumor that differentiates into germinative hair follicle cells[1-3]. Representing < 1% of all skin tumors, its clinical and histopathological similarities with BCC components pose a controversy in both dermatologic surgery and clinical settings, as this neoplasm has a rare chance of malignant transformation[3-7].

According to Rezze et al. dermoscopy is an essential technique in the clinical approach to skin lesions, playing a key role in identifying malignant lesions such as BCC[8]. However, dermoscopic findings in DT can mimic BCC structures, such as pearly shine and branching telangiectasias[9]. While arborizing telangiectasias are common in many cutaneous neoplasms, these vessels are thicker and more branched in nodular BCC, unlike the finer, less branched vessels in DT, which aligns with this patient's dermoscopic findings[9].

Histopathological findings in trichoepithelioma are characterized by basaloid cell proliferation, compact desmoplastic stroma, small cysts lined with keratinized epithelium, and sometimes calcifications. These features overlap with BCC, necessitating immunohistochemical studies for definitive diagnosis, as trichoepithelioma does not express carcinoembryonic antigen[10-14].

Studies like Bains et al. used markers CK20, Ki-67, Bcl-2, CD10, and CD34 in immunohistochemistry to evaluate reactivity between the two neoplasms discussed. However, CD34, CD10, and CK20 markers were not used in this case; only Bcl-2 and Ki-67 were applied[15]. The Ki-67 marker showed 5-10% tumor cell proliferation, consistent with Bains et al.'s findings, while Bcl-2 did not show reactivity, highlighting the need to define an immunohistochemical panel to differentiate this benign tumor from other malignant neoplasms[15].

Given this, there is limited scientific evidence on trichoepithelioma and its variants, especially the desmoplastic form, as it is a rare neoplasm with low population incidence. Only one publication exists in Brazilian literature.

Furthermore, few studies address specific markers for identifying and differentiating this disease. Thus, continuous monitoring of suspected DT lesions is crucial to correctly rule out malignant cutaneous diagnoses and implement appropriate therapeutic management.

Conclusion

The patient in this case report presents with DT, a rare but benign tumor that clinically and histopathologically resembles BCC. Immunohistochemistry is an essential and necessary test for diagnostic confirmation and for defining the appropriate therapeutic management. In addition, there is limited literature evaluating the desmoplastic form of trichoepithelioma and its histological or immunohistochemical diagnosis. Therefore, careful attention is needed to avoid diagnostic errors and unnecessary treatments for patients diagnosed with this condition.

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 (AI). 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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CASE REPORT

Angiosarcoma: clinical and histopathological characterization of five cases and literature review

Angiossarcomas: caracterização clínica e histopatológica de cinco casos e revisão da literatura

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Abstract

Angiosarcomas are rare, aggressive endothelial tumors, accounting for < 1% of all sarcomas. These tumors predominantly affect elderly Caucasian men and often occur on the face, scalp, or in areas of chronic lymphedema or previous radiotherapy exposure. Early diagnosis is essential due to their high recurrence and metastasis rates. This study aims to describe and analyze five cases of cutaneous angiosarcoma diagnosed at a tertiary hospital in Lisbon, highlighting clinical presentations and the importance of timely diagnosis. We reviewed five cases of cutaneous angiosarcoma diagnosed between 2014 and 2023 at a tertiary hospital. Data on demographics, clinical presentation, and tumor location were retrospectively collected and analyzed. The sample included five patients: three females and two males, with a mean age of 75.8 years. Lesions presented as erythematous and violaceous patches, plaques, and nodules across various anatomical sites. The findings emphasize the diversity of clinical presentations and underscore the need for a high index of suspicion among dermatologists. Due to the aggressive nature of angiosarcomas, dermatologists must maintain a high level of suspicion for early diagnosis, which can improve outcomes. In addition, there is an urgent need to develop novel therapeutic strategies to manage these tumors effectively.

Keywords: Cutaneous angiosarcomas. Endothelial tumors. Sarcomas.

Resumo

Os angiossarcomas são tumores endoteliais raros e agressivos, representando menos de 1% de todos os sarcomas. Estes tumores afetam predominantemente homens caucasianos idosos e surgem com maior frequência na face, couro cabeludo ou em áreas de linfedema crónico ou previamente expostas a radioterapia. O diagnóstico precoce é essencial devido às elevadas taxas de recidiva e metastização. Este estudo tem como objetivo descrever e analisar cinco casos de angiossarcoma cutâneo diagnosticados num hospital terciário em Lisboa, destacando a apresentação clínica e a importância de um diagnóstico atempado. Foram revistos cinco casos de angiossarcoma cutâneo diagnosticados entre 2014 e 2023 num hospital terciário. Recolheram-se e analisaram-se retrospetivamente dados demográficos, apresentação clínica e localização tumoral. A amostra incluiu cinco doentes: três do sexo feminino e dois do sexo masculino, com uma idade média de 75,8 anos. As lesões apresentaram-se sob a forma de máculas e placas eritematosas e violáceas, bem como nódulos, distribuídos por diferentes localizações anatómicas. Os resultados evidenciam a diversidade das apresentações clínicas e salientam a

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necessidade de um elevado índice de suspeição por parte dos Dermatologistas. Devido ao comportamento agressivo dos angiossarcomas, é fundamental que os Dermatologistas mantenham um elevado grau de suspeição para permitir um diagnóstico precoce, o que pode melhorar o prognóstico. Além disso, existe uma necessidade urgente de desenvolver novas estratégias terapêuticas para um tratamento mais eficaz destes tumores.

Palavras-chave: Angiossarcomas cutâneos. Tumores endoteliais. Sarcomas.

Introduction

Despite their rarity, angiosarcomas are among the more common forms of cutaneous sarcomas, ranking fourth after Kaposi's sarcoma, dermatofibrosarcoma protuberans, and pleomorphic dermal sarcoma[1,2]. These tumors are highly aggressive and present significant diagnostic and therapeutic challenges due to their variable clinical presentations.

Three types of angiosarcoma have been identified: primary, associated with chronic lymphedema, and post-radiation[1-3]. The most common type is primary angiosarcoma (idiopathic or Wilson-Jones), which mainly affects Caucasian men over 70 years old. It usually presents on the head and neck regions as a single lesion resembling an innocent hematoma[1,2]. Angiosarcoma associated with chronic lymphedema presents as firm violaceous nodules or hardened plaques on a background of non-pitting edema; more than 90% of these cases are associated with mastectomy and lymph node dissection in women with breast cancer (Stewart-Treves syndrome)[1,2]. Lymphedema precedes the appearance of angiosarcoma in 4-27 years[1-3]. Post-radiation angiosarcomas manifest as infiltrating plaques or nodules in or near the irradiated area, approximately 6 years after treatment[1-3].

Awareness among dermatologists is crucial for early diagnosis, as long-term survival largely depends on prompt radical surgery and adjuvant radiotherapy. This series describes the clinical and histopathological characteristics of the five cases of cutaneous angiosarcomas diagnosed over a period of 9 years in a dermatology department at a tertiary hospital in Lisbon, Portugal.

Case reports

Case 1

A 92-year-old Caucasian man presented with multiple violaceous patches, plaques, and nodules on the scalp (Fig. 1). Histopathologic examination from an incisional skin biopsy revealed an endothelial infiltrative tumor (Fig. 2). Immunohistochemistry was positive for CD31 and electroretinography (ERG). According to the 8th edition of the American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) staging system, the tumor was classified as stage I (T3N0M0). The patient underwent surgical excision but died 3 months later due to an unrelated infectious complication, before starting the proposed adjuvant radiotherapy.

Case 2

An 87-year-old woman with a history of breast cancer 17 years earlier, treated with conservative mastectomy and radiotherapy, presented with a violaceous nodule in the previously irradiated area (Fig. 3). Histopathologic examination of the surgical specimen revealed a tumor with diffuse proliferation in the dermis and subcutaneous tissue, irregular vascular clefts with fusiform endothelial cells, and cellular pleomorphism with round, epithelioid cells (Fig. 4). Immunohistochemistry was positive for CD31, podoplanin, ERG, and c-MYC. According to the AJCC (8th ed) TNM system, the tumor was staged as stage IA (T1aN0M0). Wide local excision was performed, and the patient remains alive and free of recurrence after 7 months of follow-up.

Case 3

A 57-year-old female with chronic lymphedema of the right upper limb following mastectomy and lymphadenectomy for breast cancer 18 years earlier presented with multiple coalescent bleeding violaceous plaques and nodules on the inner aspect of the right arm (Fig. 5). Histopathologic examination from an incisional skin biopsy revealed a dense infiltrative tumor with epithelioid cells, the classic "fish in the creek" pattern, and pleomorphic, undifferentiated cells (Fig. 6). Immunohistochemistry was positive for CD31 and podoplanin. According to the AJCC (8th ed) TNM system, the tumor was staged as stage IV (T4N1M0). The patient also had a concurrent stage IIIA lung carcinoma. Given her poor performance status and the extent of cutaneous disease, she received best supportive care and died within 1 month due to sepsis.

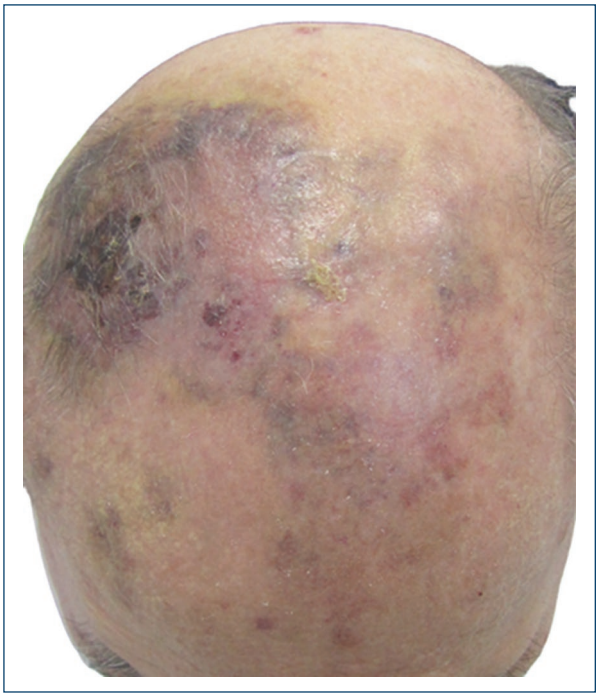

Figure 1. Physical examination showed multiple violaceous patches, plaques, and nodules on the scalp.

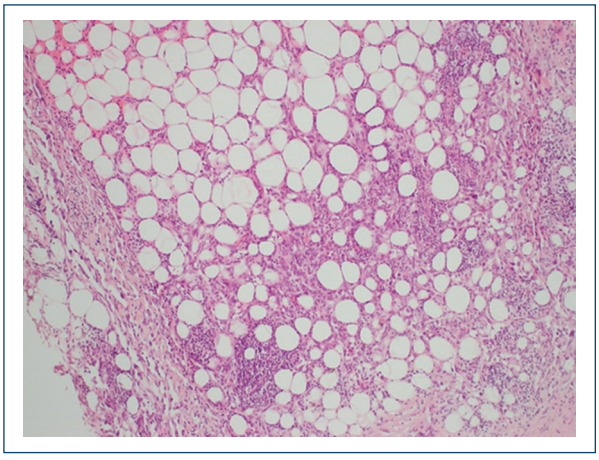

Figure 2. Histopathologic examination from an incisional skin biopsy reveals an endothelial tumor infiltrating the collagen bundles and adipose tissue (H&E, ×100).

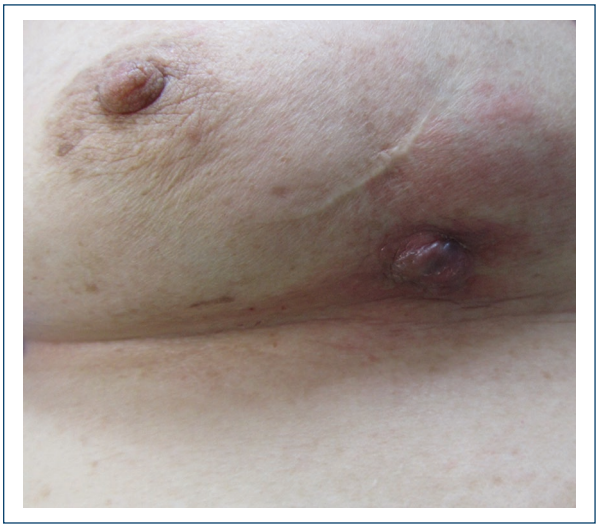

Figure 3. Physical examination showed a violaceous nodule in the left breast.

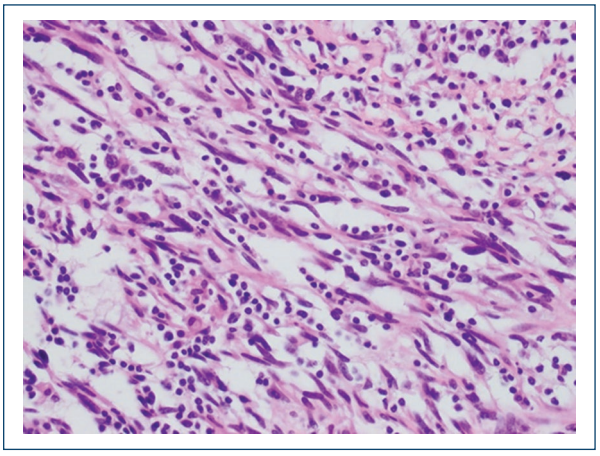

Figure 4. Histopathologic examination of the surgical specimen reveals a tumor with diffuse proliferation in the dermis and subcutaneous tissue and irregular vascular clefts (H&E, ×100).

Case 4

An 81-year-old female with chronic idiopathic lymphedema of the lower limbs presented with multiple friable coalescent bleeding nodules on the anterior aspect of the right leg (Fig. 7). Histopathologic examination from an incisional skin biopsy revealed an endothelial tumor with irregular vascular clefts and multilayering (Fig. 8). Immunohistochemistry was positive for CD31 and podoplanin. According to the AJCC (8th ed) TNM system, the tumor was staged as stage IB (T4 [multicentric] N0M0), compatible with localized inoperable disease. The patient was treated with radiotherapy and paclitaxel and survived for 13 months after diagnosis. The cause of death was unknown because of loss to follow-up.

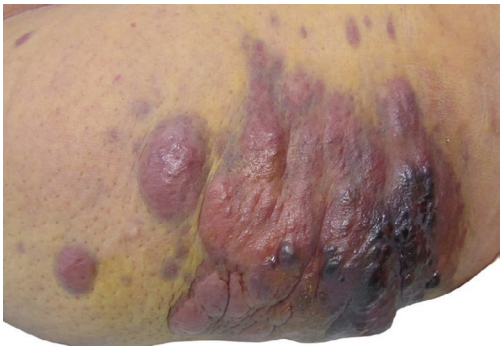

Figure 5. Physical examination showed multiple coalescent bleeding violaceous plaques and nodules in the inner aspect of the right arm.

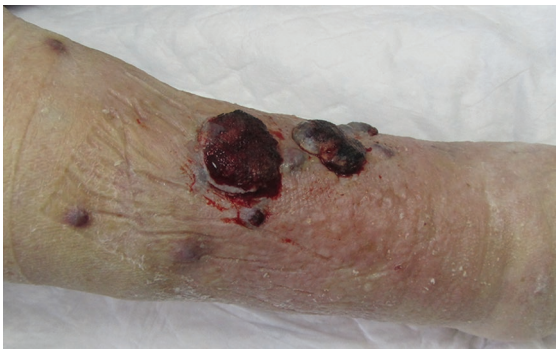

Figure 7. Physical examination showed bleeding nodules on the anterior aspect of the right leg.

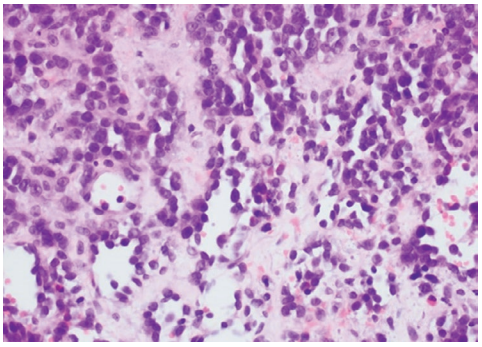

Figure 6. Histopathologic examination from an incisional skin biopsy revealed the classic "fish in the creek" sign and pleomorphic, undifferentiated cells with numerous mitoses (H&E, ×400).

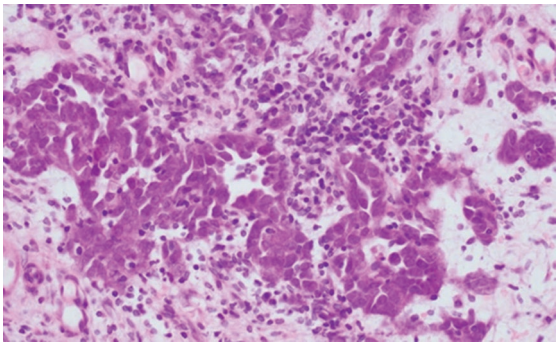

Figure 8. Histopathologic examination from an incisional skin biopsy revealed an endothelial tumor with irregular vascular clefts and multilayering (H&E, ×100).

Case 5

A 62-year-old male with a history of desmoplastic melanoma 12 years earlier and three local recurrences presented with a pink nodule in the previous surgical scar. Histopathologic examination of the surgical specimen revealed irregular vascular clefts dissecting between collagen bundles (Fig. 9). Immunohistochemistry was positive for CD31. According to the AJCC (8th ed) TNM system, the tumor was staged as stage IA (T1aN0M0). The patient underwent surgery, radiotherapy, and paclitaxel treatment. Despite these interventions, surgical margins remained positive, with local recurrences and locoregional lymph node involvement over time. He subsequently received systemic therapy with gemcitabine, doxorubicin, and pazopanib, but was

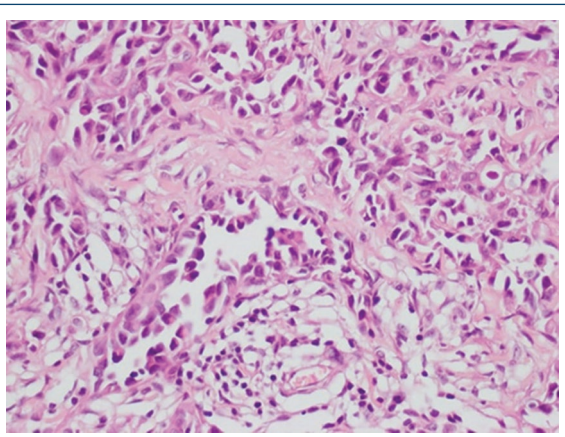

Figure 9. Histopathologic examination of the surgical specimen revealed irregular vascular clefts dissecting between the collagen bundles (H&E, ×100).

later lost to follow-up and died 6 years and 5 months after diagnosis, with an unknown cause of death.

Results

We identified five cases of cutaneous angiosarcomas: two idiopathic (40%), two associated with chronic lymphedema (40%), and one post-radiation (20%). There were three female (60%) and two male (40%) patients. The mean age of our patients was 75.8 (standard deviation [SD] 13.8; range 57-92) years. The tumors were found in various locations, including the breast, trunk, limbs, and scalp, presenting as erythematous and violaceous patches, plaques, and nodules. Our analysis revealed a mean follow-up of 20 months and a mean overall survival of 23.5 months. Four out of the five patients (80%) died during the follow-up period.

Discussion

In our sample, the two most common types of cutaneous angiosarcoma were primary angiosarcoma and angiosarcoma associated with chronic lymphedema, followed by post-radiation angiosarcoma. These results differ from the literature, which most frequently reports primary angiosarcoma, followed by post-radiation angiosarcoma, and angiosarcoma associated with chronic lymphedema. The average age of our patients was consistent with data from the literature, indicating that most cases occur in elderly patients. Angiosarcomas are more common in males, but in our study 60% of the patients were female. The locations described in our analysis are consistent with those reported in the literature, although the most common location is the head and neck region, where we found only one tumor. Our study showed a mean overall survival of 23.5 months, corresponding to a 9-year survival rate of 20%, which is higher than the 5-year survival rate of 12-34% reported in the literature. These discrepancies are probably related to the small size of our sample.

The first case corresponds to the classic presentation of primary angiosarcoma, highlighting the importance of maintaining a high level of suspicion for persistent erythematous and violaceous lesions in the head and neck region in elderly patients. These lesions can initially be presumed to be benign or traumatic, especially in an elderly population commonly taking antiplatelet or anticoagulant drugs.

The second case is also a typical presentation to keep in mind, emphasizing the importance of suspecting cutaneous neoplasms in patients who have undergone radiotherapy for breast cancer. The main differential diagnoses to consider in this setting are basal cell carcinoma (the most common tumor), angiosarcoma, and atypical vascular lesions of the breast[4]. Differentiating between the latter two is challenging, with the presence of positive c-MYC favoring the diagnosis of angiosarcoma, stressing the importance of immunohistochemistry. Notably, the incidence of post-radiation angiosarcomas is increasing, while the incidence of angiosarcoma associated with chronic lymphedema, mainly seen following lymphadenectomy for breast cancer (Stewart-Treves syndrome), is decreasing. This reduction is attributed to the adoption of more conservative surgical techniques, combined with radiotherapy, for breast cancer.

The third and fourth cases are classic, from both a clinical and histopathological perspective. Clinically, the appearance of erythematous and violaceous skin lesions on a background of chronic lymphedema should always raise suspicion for angiosarcoma and prompt a biopsy. Histopathologically, the “fish in the creek” sign (free-floating endothelial cells within the vascular lumen) in the third case is considered a unique histologic pattern of cutaneous angiosarcoma[5], and the multilayering in the fourth case is also typical.

The fifth case is the one showing the least common characteristics, considering the young age at presentation, the location on the back, and the history of recurrent desmoplastic melanoma in the affected site. In fact, a revision of the initial surgical specimens concluded that the lesions previously interpreted as melanoma were probably poorly differentiated angiosarcomas, misdiagnosed in an era when immunohistochemistry was not widely available. This case illustrates the clinical and histopathological diagnostic challenges of angiosarcomas.

Angiosarcomas pose two major challenges: clinical and histopathological diagnosis. Clinically, they can present as deceptively benign-appearing lesions, often in non-specific locations. Histopathologically, despite typical features, not all specimens reveal these changes[6]. The use of vascular markers in immunohistochemistry, including CD31, ERG, CD34, and Fli-1, is crucial for diagnosis[6]. ERG is currently considered the most sensitive and specific marker for angiosarcoma[7].

Despite aggressive multimodal therapy, angiosarcomas have a poor prognosis, with a 5-year survival rate of 12-34%[1,8]. Early radical surgery followed by adjuvant

radiotherapy appears crucial for improving outcomes. However, the high recurrence rate highlights the need for vigilant follow-up and possibly novel therapeutic approaches, including experimental therapy with propranolol, pembrolizumab, and the triple combination of pioglitazone with rofecoxib and trofosfamide[9-11].

Our results illustrate the wide range of clinical presentations of cutaneous angiosarcomas and their diagnostic challenges. Furthermore, they corroborate literature data, indicating that these tumors have a very poor prognosis. However, this is a study with a small number of patients and potential selection biases, so results should be interpreted cautiously. Further research with larger, more diverse cohorts is needed to validate these observations.

Conclusion

Cutaneous angiosarcomas are aggressive endothelial tumors with significant clinical and histopathological variability. This case series emphasizes the need for heightened awareness among dermatologists and oncologists regarding the diverse presentations of angiosarcomas. Early diagnosis and aggressive treatment are pivotal in managing these tumors, although the prognosis remains poor. Further research into novel therapeutic strategies and better diagnostic markers is essential to improve outcomes.

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 (AI). 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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CASE REPORT

Spitz nevus: a case report of a benign melanocytic neoplasm with a review of recent advances

Nevo de Spitz: relato de caso de uma neoplasia melanocítica benigna com revisão dos avanços recentes

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Abstract

Spitz nevus is a rare benign melanocytic lesion that can clinically mimic benign and malignant dermatological conditions. We report a case of a 22-year-old female who presented with a long-standing, asymptomatic nodule on her left cheek. The lesion was excised due to cosmetic concerns, and histopathological analysis confirmed the diagnosis of Spitz nevus. Given its clinical resemblance to malignant conditions, a complete surgical excision was performed for definitive diagnosis and cosmetic management. Recent studies highlight advances in molecular diagnostics and immunohistochemistry, which help differentiate Spitz nevus from malignant melanocytic neoplasms. This case underscores the necessity of histopathological and molecular evaluation in distinguishing Spitz nevus from other pigmented lesions.

Keywords: Nevus. Benign melanocytic tumor. Spitz tumor.

Resumo

O nevo de Spitz é uma lesão melanocítica benigna rara que pode mimetizar clinicamente condições dermatológicas benignas e malignas. Relata-se o caso de uma doente de 22 anos que apresentava um nódulo assintomático de longa data na face esquerda. A lesão foi excisada devido a preocupações estéticas, e a análise histopatológica confirmou o diagnóstico de nevo de Spitz. Dada a semelhança clínica com condições malignas, foi realizada uma excisão cirúrgica completa para diagnóstico definitivo e tratamento estético. Estudos recentes destacam os avanços no diagnóstico molecular e na imunohistoquímica, que auxiliam na diferenciação do nevo de Spitz das neoplasias melanocíticas malignas. Este caso realça a necessidade de avaliação histopatológica e molecular para distinguir o nevo de Spitz de outras lesões pigmentadas.

Palavras-chave: Nevo. Tumor melanocítico benigno. Tumor de Spitz.

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Introduction

Spitz nevus, first described by Sophie Spitz in 1948, is a benign melanocytic neoplasm commonly seen in young individuals, particularly females[1]. Clinically, it can mimic various conditions, including melanoma, basal cell carcinoma, and dermatofibroma, making histopathological examination essential for accurate diagnosis[2]. Although typically benign, complete surgical excision is often recommended due to its difficulty in differentiating it from malignant melanocytic lesions[3].

Case report

A 22-year-old female presented to the dermatology outpatient department with a solitary lesion on her left cheek, which had been present for 4 years. The lesion developed insidiously without any preceding history of trauma, insect bites, or inflammation. The patient had no significant personal or family history of skin disorders. She sought medical attention due to cosmetic concerns.

On dermatological examination, the lesion was a well-circumscribed, firm, dome-shaped, oval nodule measuring approximately 1.0 cm × 1.5 cm (Fig. 1). The lesion had a slightly pink hue with mild hyperpigmentation in the centre. The surface was smooth without ulceration, scaling, or crusting. The lesion was not fixed to the underlying structures, and there was no regional lymphadenopathy. Sensory and motor examinations were unremarkable.

Based on the clinical presentation, the differential diagnoses included intradermal nevus, desmoplastic nevus, melanoma, basal cell carcinoma, dermatofibroma, pseudolymphoma, and histoid leprosy.

The lesion was completely excised with primary closure. The excised tissue was sent for histopathological evaluation. Hematoxylin and eosin staining revealed a well-circumscribed dermal lesion composed of large spindle-shaped melanocytic cells arranged in nests (Fig. 2). The nevus cells were symmetrically placed with well-defined clefts between the junctional nests and the surrounding epidermis (Fig. 3). There was mild pigment incontinence, but no cellular atypia or mitotic figures were observed. These findings were consistent with a diagnosis of Spitz nevus.

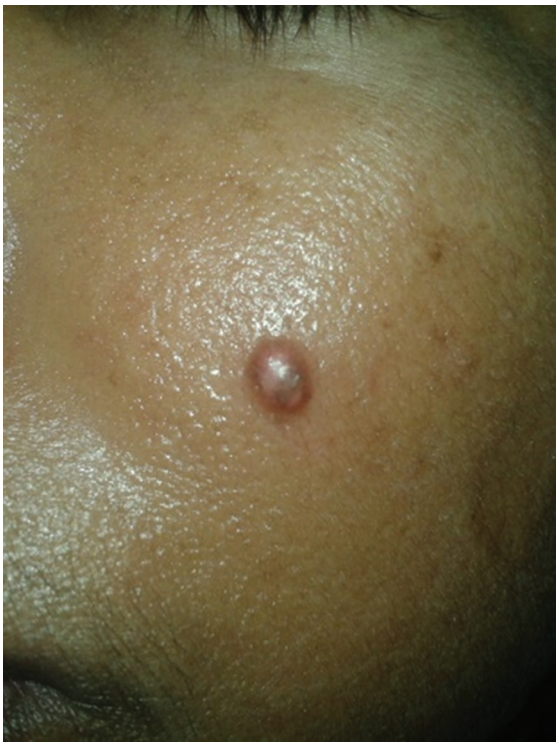

Figure 1. A well-circumscribed dome-shaped nodule on the left side of the face.

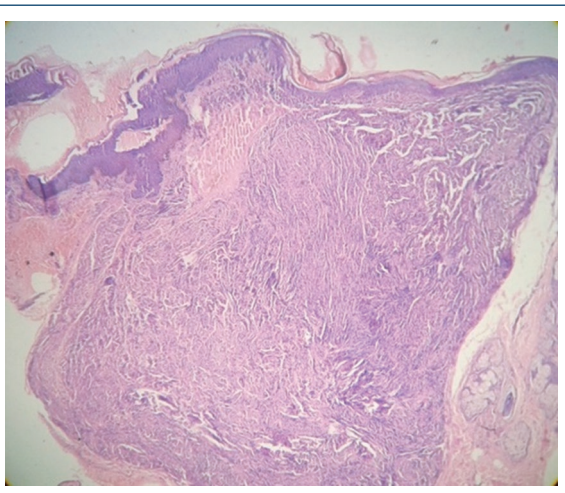

Figure 2. H&E stain (×10 magnification) showing well-circumscribed junctional and dermal nest of spindled-shaped melanocytic cells.

Discussion

Spitz nevus is a benign melanocytic proliferation that primarily occurs in children and young adults[1]. It is characterized by the spindle and epithelioid melanocytes arranged in nests within the dermis or at the dermo-epidermal junction[3]. Clinically, it can be confused with malignant melanocytic lesions, necessitating histopathological confirmation[2].

Spitz nevus can exhibit a range of histopathological patterns, including conventional (classic), desmoplastic, pigmented, and angiomatoid subtypes[4]. The presence of clefts separating the nevus cells from the epidermis and a well-circumscribed symmetrical

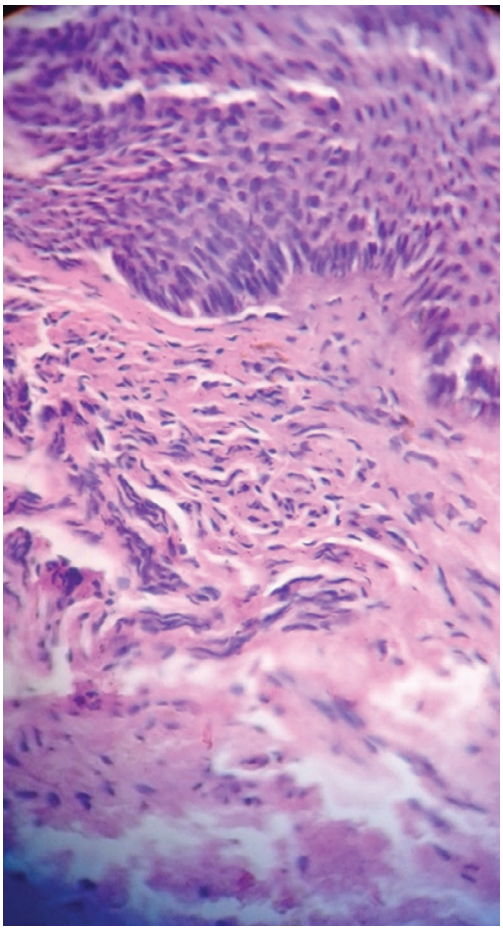

Figure 3. H&E stain (×40 magnification) showing clefts in between the nests of spindle-shaped nevus cells.

arrangement are distinguishing features[4]. Unlike malignant melanomas, Spitz nevi typically lack significant cellular atypia and mitotic activity[5].

While Spitz nevus is generally considered benign, rare cases of atypical Spitz tumors with uncertain malignant potential have been reported, necessitating long-term follow-up in select cases[3]. Recent studies suggest that immunohistochemical markers such as p16, Ki-67, and HMB-45 can aid in distinguishing Spitz nevi from malignant melanomas[6]. In addition, molecular techniques, such as FISH and CGH are proving useful in differentiating atypical Spitz tumors from other melanocytic proliferations[7]. The use of molecular markers, such as HRAS mutations and gene fusions, has been identified in Spitz nevi, offering a new avenue for diagnostic refinement[7].

The standard treatment for Spitz nevus is complete surgical excision, both for diagnostic purposes and to prevent misdiagnosis[8].

Conclusion

This case highlights the importance of considering Spitz nevus in the differential diagnosis of solitary pigmented nodules, especially in young individuals. Given its potential for clinical confusion with malignant lesions, histopathological and molecular confirmations remain the gold standard for diagnosis. Complete surgical excision is the preferred management approach for both diagnostic accuracy and cosmetic concerns. The incorporation of molecular and immunohistochemical techniques can enhance diagnostic precision and improve patient management.

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 (AI). 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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CASE REPORT

Mycophenolate mofetil in refractory discoid lupus erythematosus. Case report and literature review

Micofenolato de mofetil no lúpus eritematoso discoide refratário. Relato de um caso e revisão da literatura

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Abstract

Discoid lupus erythematosus (DLE) is a chronic autoimmune disease affecting the skin, often leading to scarring, dyspigmentation, and reduced quality of life. Although several first-line therapies are available, some cases remain refractory. We report a 53-year-old female with treatment-resistant DLE, presenting with cicatricial alopecia and plaques on the face, torso, and limbs. Histopathology confirmed the diagnosis. Conventional therapies – including corticosteroids, hydroxychloroquine, prednisolone, methotrexate, acitretin, and dapsone – failed to provide lasting control. Treatment with mycophenolate mofetil (MMF) achieved significant clinical improvement and stabilization over 15 months, with good tolerability. This case illustrates the challenges of managing refractory DLE and suggests MMF as a potential therapeutic option. A literature review reveals limited yet encouraging evidence from retrospective studies and case reports supporting MMF's efficacy in refractory DLE. Further scientific evidence is needed to establish its role in clinical practice and guide treatment for patients with severe or treatment-resistant DLE.

Keywords: Discoid lupus erythematosus. Refractory cutaneous lupus. Mycophenolate mofetil. Autoimmune skin disease. Cicatricial alopecia. Immunosuppressive therapy.

Resumo

O Lúpus Eritematoso Discóide (LED) é uma dermatose autoimune crónica que causa alterações cicatriciais e redução da qualidade de vida. Apesar das terapêuticas de primeira linha disponíveis, alguns casos mantém-se refratários. Apresentamos o caso de uma mulher, 53 anos, com alopécia cicatricial e placas no rosto, tronco e membros. O exame histopatológico confirmou o diagnóstico de LED. Tratamentos prévios – incluindo corticosteroides tópicos, hidroxicloroquina, prednisolona oral, metotrexato, acitretina e dapsona – não permitiram controlo da dermatose. O tratamento com micofenolato de mofetil (MMF) resultou numa melhoria significativa e estabilização das lesões durante 15 meses, com boa tolerabilidade. Este caso ilustra os desafios na abordagem do LED refratário e sugere o MMF como opção terapêutica. Uma revisão da literatura revelou evidência limitada mas encorajadora, com base em estudos retrospectivos e relatos de caso. É necessária mais evidência científica para clarificar o papel do MMF e criar recomendações terapêuticas para doentes com LED grave/refratário.

Palavras-chave: Lúpus eritematoso discoid. Lúpus cutâneo refratário. Micofenolato de mofetil. Doenças autoimunes. Alopécia cicatricial. Tratamento imunossupressor.

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Introduction

Lupus erythematosus is an autoimmune disease that commonly affects the skin. It encompasses a spectrum of different cutaneous manifestations, among which discoid lupus erythematosus (DLE) is one of the most common among chronic forms. DLE often manifests as scaly, erythematous plaques with potential permanent scarring and pigmentary changes, significantly impacting patients' quality of life. It predominantly affects photoexposed sites, such as the face and scalp, although lesions may occur in other locations. DLE may signal systemic lupus erythematosus (SLE) in a subset of cases, particularly in the generalized form. Treatment of DLE may prove difficult, and delaying effective treatment can lead to permanent scarring and disfiguration.

Case report

A 53-year-old Caucasian female patient, smoker, with no other relevant medical history was referred to the Dermatology Clinic with a 1-year history of alopecia and erythematous lesions on the face.

On physical examination, an extensive erythematous infiltrated plaque of cicatricial alopecia was observed across almost the entire sagittal region, with peripheral hyperpigmentation. The patient also presented two well-defined erythematous plaques, on the left malar and glabellar region, with central scaling and peripheral hyperpigmentation.

The patient had no other complaints and an unremarkable complete blood count and biochemical panel, as well as an antinuclear antibodies test of 1:80, negative anti-double-stranded DNA antibody, and serum complement levels (C3 and C4) within the reference range, making the presence of systemic disease unlikely.

A 6 mm punch skin biopsy was performed on the scalp, showing areas of follicular keratosis in the epidermis, with vacuolar degeneration in the basal layer and acidophilic bodies. There was a dermal perivascular and periadnexial lymphohistiocytic infiltrate (Figs. 1 and 2). These findings were consistent with the clinical diagnosis of discoid cutaneous lupus erythematosus.

The patient was initially treated with topical betamethasone and strict photoprotection, with no improvement and even with the appearance of new lesions on the face, trunk, and upper limbs. Given the widespread nature of lesions, intralesional corticosteroid therapy was not proposed, and the patient was started on hydroxychloroquine 400 mg daily and a course of oral prednisolone, with transient improvement but worsening during tapering. At this point, oral methotrexate was added and titrated up to 15 mg weekly, with subsequent discontinuation due to moderate gastrointestinal intolerance and lack of response. Therapeutic trials with acitretin 10 mg daily and dapsone, titrated to 100 mg daily, were also conducted, but both were unsuccessful, with an increase in lesion size. We later started treatment with mycophenolate mofetil (MMF), titrated up to 2 g/day, which finally allowed control of the disease, with improvement of inflammatory signs of the lesions and stabilization of their size. Complete blood count,

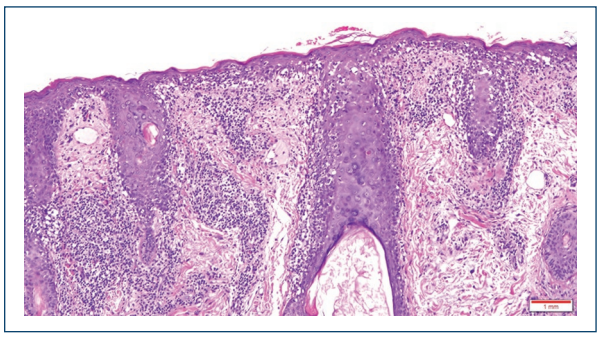

Figure 1. (H&E ×40) Epidermis with follicular keratosis and areas of vacuolar degeneration of the basal layer. In the dermis, a superficial and deep perivascular lymphohistiocytic and periadnexal inflammatory infiltrate is observed. There is also vascular dilation and foci of interstitial hemorrhage.

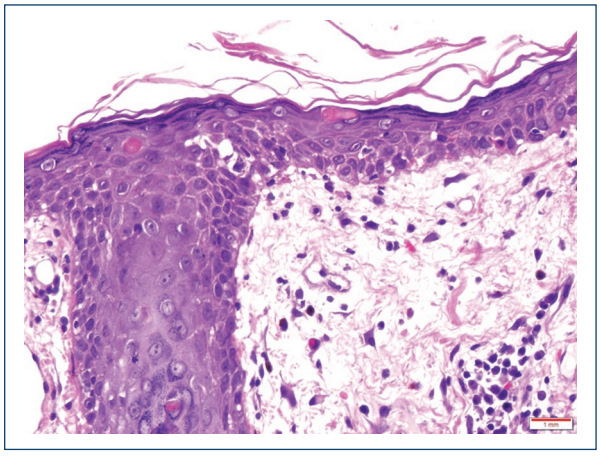

Figure 2. (H&E ×400) Higher amplification, showcasing follicular keratosis, vacuolar degeneration of the basal layer, and the presence of acidophilic bodies.

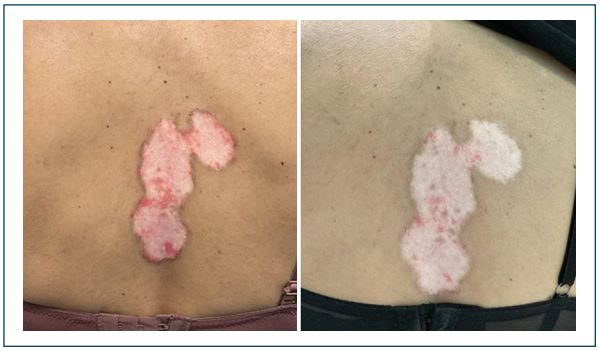

Figure 3. Lesions of discoid lupus erythematosus on the back before (left) and after (right) 10 months of therapy with mycophenolate mofetil.

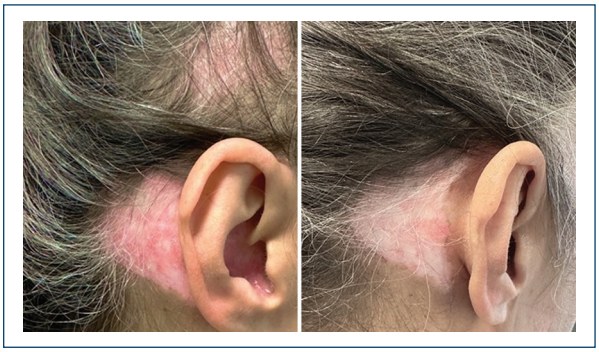

Figure 5. Right retroauricular lesions of discoid lupus erythematosus before (left) and after (right) 10 months of therapy with mycophenolate mofetil.

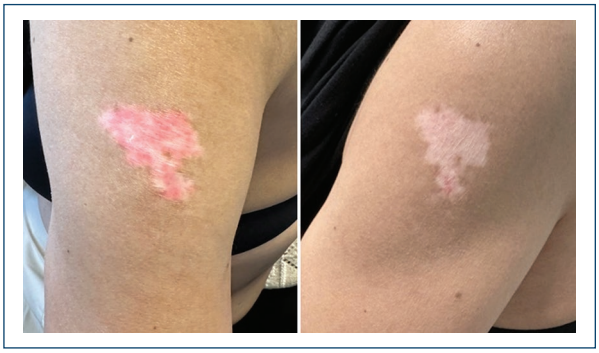

Figure 4. Lesions of discoid lupus erythematosus on the left arm before (left) and after (right) 10 months of therapy with mycophenolate mofetil.

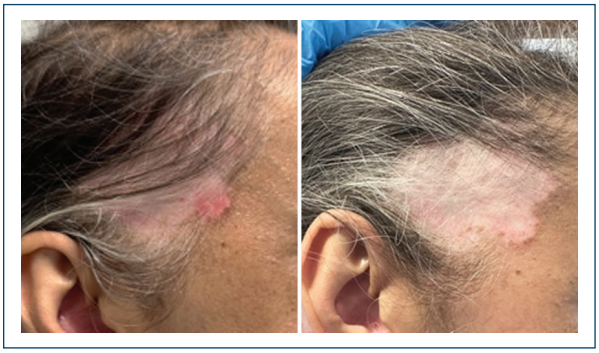

Figure 6. Right frontotemporal lesions of discoid lupus erythematosus before (left) and after (right) 10 months of therapy with mycophenolate mofetil.

liver enzymes, and renal function were assessed 2 weeks after treatment initiation and subsequently repeated every other month, with progressive spacing of follow-up laboratory evaluations. No new lesions developed after the patient was started on MMF and there was very significant clinical improvement after 10 months of therapy with MMF in several locations (Figs. 3-10). The treatment was well tolerated, with no reported side effects. The patient maintains follow-up and remains without disease activity 15 months after initiating treatment.

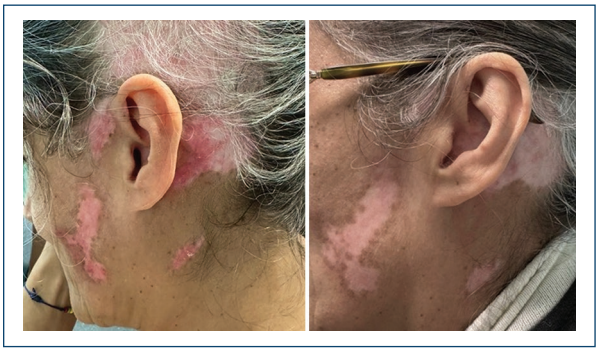

Figure 7. Left facial and retroauricular lesions of discoid lupus erythematosus before (left) and after (right) 10 months of therapy with mycophenolate mofetil.

Discussion

To date, there are no well-established therapeutic guidelines for cutaneous lupus refractory to first-line drugs, including DLE. Fortunately, most patients respond to treatment with topical/intralesional corticosteroids, topical calcineurin inhibitors, oral anti-malarial drugs, and photoprotection. The generalized forms of DLE increase the risk of SLE and may prove more difficult to treat.

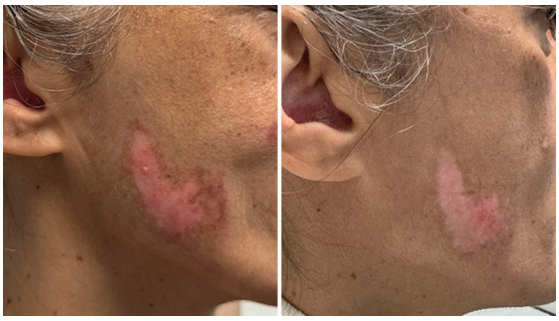

Figure 8. Right mandibular lesions of discoid lupus erythematosus before (left) and after (right) 10 months of therapy with mycophenolate mofetil.

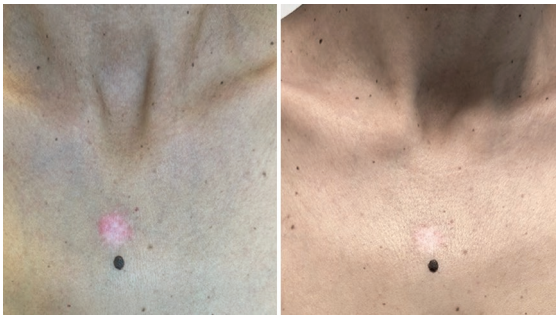

Figure 9. Presternal lesion of discoid lupus erythematosus before (left) and after (right) 10 months of therapy with mycophenolate mofetil.

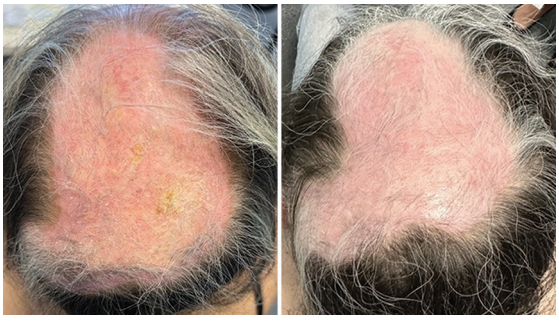

Figure 10. Scalp lesion of discoid lupus erythematosus before (left) and after (right) 10 months of therapy with mycophenolate mofetil.

MMF is an immunosuppressant drug that is generally well tolerated and reversibly inhibits the enzyme inosine monophosphate dehydrogenase (involved in the synthesis of purines). Diarrhea, vomiting, nausea, and low cellular blood count levels are the most common side effects[1].

There is limited evidence of the benefit of MMF in cutaneous lupus, including DLE, consisting only of retrospective studies and case reports. Furthermore, most studies tend to include in their cohort patients with several subtypes of cutaneous lupus. Even though most treatment recommendations assemble several forms of cutaneous lupus, it is not certain that all disease subtypes share the same response to a given treatment.

We reviewed all publications available at the MEDLINE database regarding the use of MMF in DLE, excluding papers that included exclusively other forms of cutaneous lupus and focusing on the results of the subset of patients diagnosed with DLE. A 2021 retrospective study from Keyes et al. showed similar results in patients with discoid or subacute cutaneous lupus treated with either methotrexate or MMF. However, their results showed a trend favoring treatment with MMF in the 40 patients with DLE, albeit with no statistical significance[2]. In another retrospective study from 2019, including patients with both subacute and discoid lupus, Gammon B. and colleagues found some improvement after MMF treatment in all 19 subjects with DLE. Regarding these 19 cases, eight patients showed a complete response to treatment, defined as complete or near-complete resolution of disease activity; eight patients had a partial response; and three patients had complete responses followed by flares of the disease[3]. Contradictorily, a former retrospective study from 2005, including three patients with DLE treated with MMF, concluded that the drug was ineffective in these patients, highlighting one case of disease flare after starting the drug[4].

The remaining evidence consists only of case series and case reports, accounting for a total of five cases with complete or near-complete responses to treatment with MMF - three patients with a palmoplantar variant of DLE[5,6], one case of lupus profundus[7], and one case of DLE associated with chilblain lupus[7]. Bardazzi et al. refer that MMF may be an effective treatment option in patients with palmoplantar disease; a rare variant that commonly has a poor response to treatment[5].

This case aims to illustrate the difficulty of treating refractory DLE and supports a potential role of MMF in refractory disease. The literature review showed a lack of substantial evidence for the use of MMF in DLE, and the comprehension of the role of this drug is further aggravated by the fact that most studies include only patients with disease refractory to the most common treatment modalities (including topical therapies, hydroxychloroquine, and methotrexate) and, in some

case, other second and third line options. This bias is emphasized by most of the cited authors. As mentioned previously, the inclusion of all subtypes of cutaneous lupus may act as a confounding factor. Keyes et al. hint at a possible difference in response to MMF among patients with DLE, compared to patients with subacute cutaneous lupus erythematosus[2]. Further studies, ideally randomized trials, are needed to clarify the role of this drug in DLE and other forms of cutaneous lupus.

Conclusion

This case highlights the therapeutic challenge posed by refractory discoid lupus erythematosus and illustrates the potential effectiveness and tolerability of mycophenolate mofetil in achieving sustained disease control after failure of multiple conventional therapies. Although current evidence remains limited to retrospective studies and case reports, our findings add to the growing body of literature suggesting a role for mycophenolate mofetil in selected patients with severe or treatment-resistant DLE. Well-designed prospective studies are needed to better define its efficacy, optimal positioning, and long-term safety in this patient population.

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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 (AI). 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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DERMATOLOGY IMAGES

Basalioma in a nevus sebaceous of the scalp

Basalioma em nevo sebáceo do couro cabeludo

Mélissa Mendes-de Carvalho and Leandro Silva*

Department of Dermatology and Venereology, Unidade Local de Saúde de Lisboa Ocidental, Lisbon, Portugal

We present the case of a 56-year-old woman with a congenital yellowish lesion on her scalp that had remained stable until approximately 18 months before evaluation. During this period, she noted the appearance of new growths on the lesion, which exhibited progressive enlargement and occasional spontaneous bleeding. On physical examination, a sessile, yellow-brown, verrucous plaque with well-defined, irregular borders, measuring approximately 4 × 1.5 cm, was observed on the interparietal scalp (Fig. 1). At the anterior margin of the plaque, a violaceous nodule with macroscopic telangiectasias, measuring approximately 1.5 cm in its greatest dimension, was identified (Fig. 1). Posterior to this, an 8-mm violaceous papule with similar features was noted (Fig. 1). Dermoscopy revealed telangiectasias and a bluish coloration (Fig. 2). Surgical excision of both lesions was performed, and histopathological examination confirmed basal cell carcinoma (BCC) arising within a nevus sebaceous, with clear surgical margins.

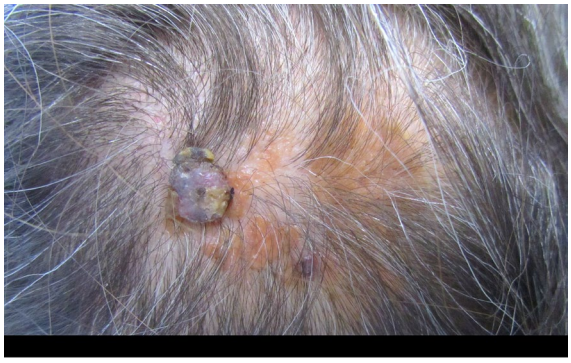

Figure 1. Physical examination showing a sessile, yellow-brown, verrucous plaque with well-defined, irregular borders, measuring approximately 4 × 1.5 cm on the scalp. Anteriorly, a violaceous nodule with macroscopic telangiectasias measures approximately 1.5 cm at its greatest dimension, and posteriorly, an 8-mm violaceous papule is present.

Nevus sebaceous, also known as nevus sebaceous of Jadassohn, is a hamartomatous lesion originating from follicular, sebaceous, apocrine, and connective tissue components[1,2]. These lesions typically present at birth or in early childhood, often as yellow to orange patches or plaques with associated alopecia[1]. While the scalp is the most common site, nevus sebaceous can also occur on the face, neck, and other regions[1]. Although predominantly congenital, sporadic cases have been documented, sometimes associated with genetic syndromes, such as Schimmelpenning-Feuerstein-Mims syndrome[1].

The clinical morphology of nevus sebaceous evolves with age. In childhood, the lesion is generally stable, appearing as a smooth or slightly raised patch[1]. Hormonal changes during puberty often lead to thickening and a more verrucous appearance[1]. Significant

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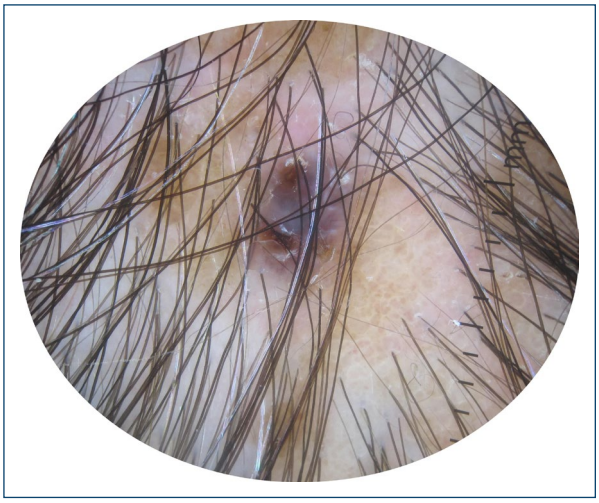

Figure 2. Dermoscopy reveals peripheral telangiectasias and a bluish coloration.

morphological changes, such as rapid growth, ulceration, or spontaneous bleeding, should prompt further evaluation, including biopsy, to exclude malignant transformation.

Nevus sebaceous carries a lifetime risk of secondary neoplasms, estimated at 10-20%[2]. Most secondary neoplasms are benign and of follicular origin[3], such as trichoblastomas or sebaceomas. Malignant transformation is rare, occurring in < 1% of cases, with BCC being the most commonly reported malignancy, followed by squamous cell carcinoma and sebaceous carcinoma[1]. When malignant neoplasms develop, they typically present in adulthood[2], as demonstrated in this case.

Histopathological confirmation of BCC arising within a nevus sebaceous is essential for guiding appropriate treatment. Surgical excision with histologically confirmed clear margins is the preferred management approach. Complete excision minimizes the risk of recurrence and allows for histopathological assessment of the entire lesion to rule out additional neoplastic changes. Clinical follow-up is recommended to monitor for recurrence or the emergence of new neoplasms.

This case emphasizes the importance of vigilance in monitoring nevus sebaceous for signs of malignant transformation. The development of new nodules, spontaneous bleeding, or ulceration should prompt immediate evaluation and intervention. Early detection and management of neoplastic transformation are critical to improving patient outcomes. Our case highlights the necessity of clinical and histopathological correlation in managing nevus sebaceous and emphasizes the importance of regular follow-up for these patients.

Author contributions

M. Mendes-de Carvalho: manuscript preparation and elaboration. L. Silva: acquisition of clinical images and critical review of the manuscript.

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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 (AI). 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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DERMATOLOGY IMAGES

Acanthosis nigricans of the ears: clinical and dermoscopy correlation

Acantose nigricante nos pavilhões auriculares: correlação clínica e dermatoscópica

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Acanthosis nigricans is a dermatological condition characterized by the presence of dark, thick, velvety, bilaterally symmetrical plaques on the skin, primarily occurring in body folds, such as neck, armpits, and groin[1], as seen in a 32-year-old obese, diabetic, male who complained of darkness over the bilateral ear lobules for 2 months (Fig. 1). Dermoscopy revealed the presence of linear crista cutis, sulcus cutis with scattered black or dark brown dots, papillary projections, and crypts (Fig. 2). Upon investigating the patient had a high body mass index, high fasting insulin levels, and S. HbA1c. Vitamin D_3 and Vitamin B12 were reduced along with a deranged lipid profile. Thyroid (72.1 µU/ml - normal 2.6-24.9 µU/ml) function tests were within normal limits. Clinical examination and a simple non-invasive bedside test, such as dermoscopy, led to a diagnosis of acanthosis nigricans. Treatment[2] included weight reduction through lifestyle modifications including dietary changes and regular physical activity, topical application of glycolic acid and urea-based cream over dark areas, regular use of sunscreen twice daily, Glycolic Acid 35% peel over neck once monthly, Vitamin D_3 and Vitamin B12 supplements, and Metformin 750 mg once a day.

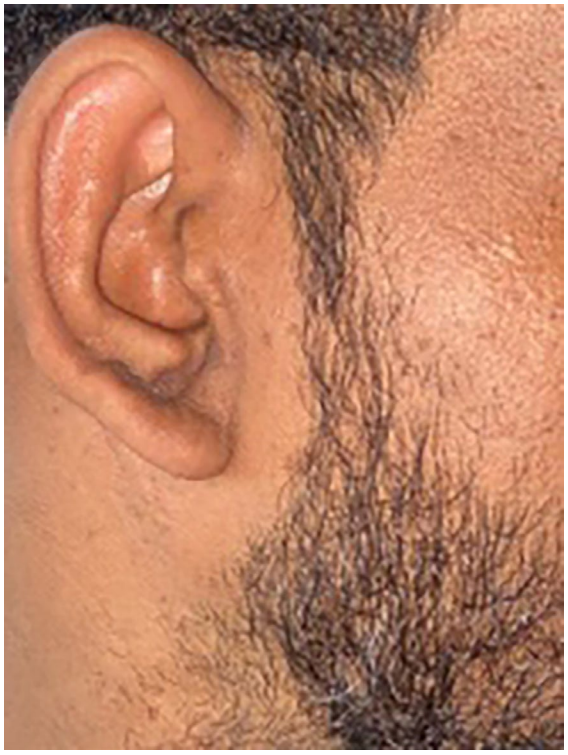

Figure 1. Thick, hyperpigmented, velvety plaque on right ear lobule.

To conclude, this case is different as the patient has acanthosis on an unusual site such as lobules of both ears and it was associated with insulin resistance, diabetes, obesity, dyslipidemia, and Vitamin D_3 and Vitamin B12 deficiency. Therefore, in rare site presentation, a high index of suspicion should arise and an extensive workup is recommended as it may be associated with metabolic syndrome.

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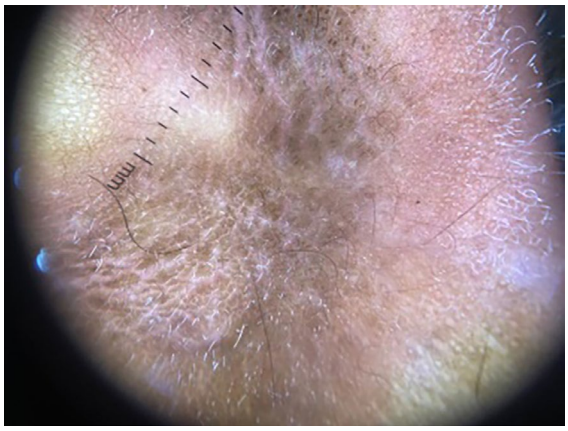

Figure 2. Polarized dermoscopy, ×200 magnification, linear crista cutis, sulcus cutis with scattered black or dark brown dots, papillary projections, and crypts.

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Ethical considerations

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DERMATOLOGY IMAGES

A giant inguinal dermatofibrosarcoma protuberans

Dermatofibrosarcoma protuberante gigante da região inguinal

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A 41-year-old male presented with an asymptomatic lesion on his groin that had been gradually enlarging over 5 years. On physical examination, a 12 × 7 cm slightly indurated, flesh-colored plaque with pedunculated nodules was observed in the left inguinal region (Fig. 1). Histopathological examination of a biopsy showed a tumor with diffuse infiltration of the skin and subcutaneous tissue composed of uniform and medium-sized spindle cells with a storiform or cartwheel pattern of growth (Fig. 2), consistent with dermatofibrosarcoma protuberans (DFSP). Staging showed no evidence of secondary lesions. Given the tumor's size and risk of functional impairment, the patient was started on therapy with imatinib. At the 6-week follow-up, the lesion remained stable.

DFSP is a rare, slow-growing, and locally aggressive soft-tissue tumor[1]. DFSP primarily affects adults, with a peak incidence between 30 and 50 years, and shows a slight male predominance[1,2]. The tumor most commonly occurs on the trunk, followed by proximal extremities and, less frequently, the head and neck[1]. Clinically, it presents as a firm, indurated, nodular, and flesh-colored or violaceous plaque that may initially resemble benign skin lesions, leading to delayed diagnosis[3]. Despite its indolent behavior, DFSP has a high propensity for local recurrence if not completely excised[1,3].

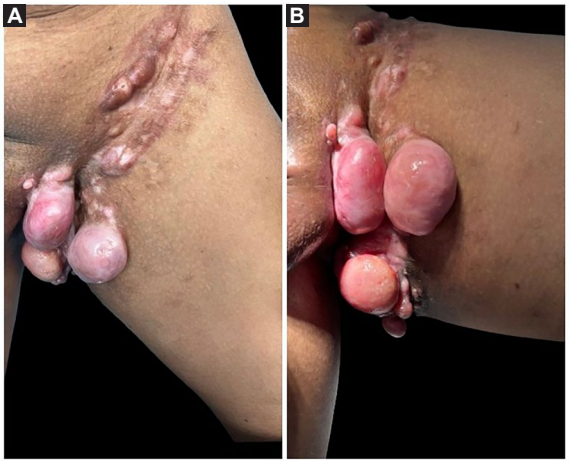

Figure 1. Clinical images with an indurated, flesh-colored plaque with several pedunculated nodules in the left inguinal region (**A:** frontal and **B:** medial views).

Wide local excision with histologically clear margins remains the treatment of choice[4]. Imatinib is an option for patients with unresectable, recurrent, and/or metastatic disease, as well as an alternative to radical surgery in select cases[5]. While metastasis is rare, recurrence poses significant challenges, requiring long-term follow-up[1].

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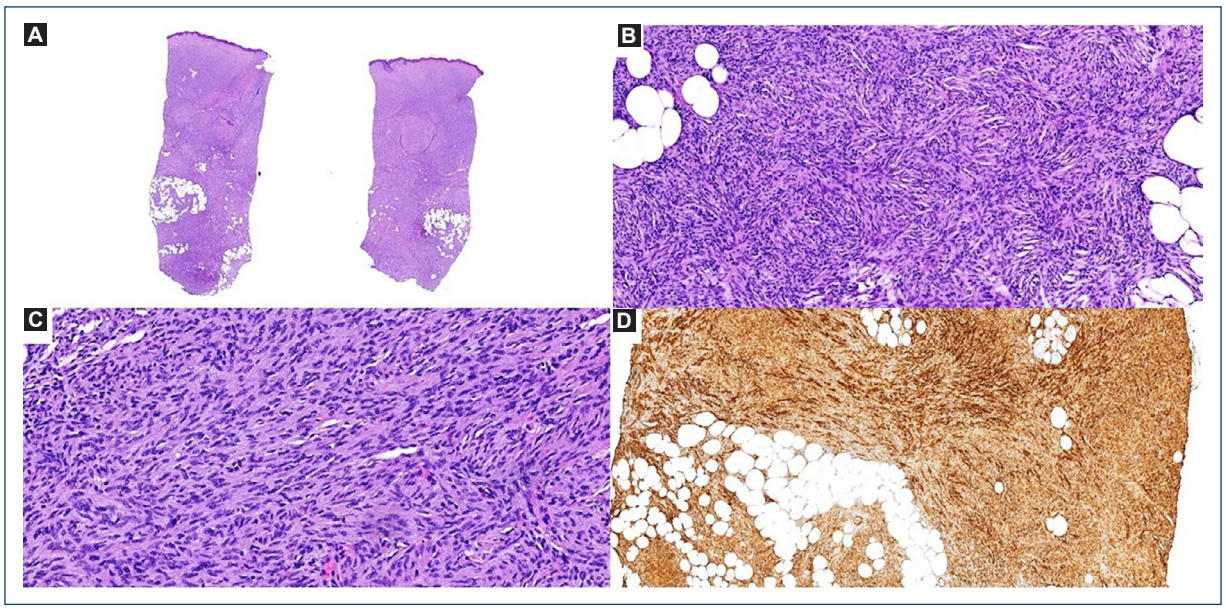

Figure 2. Dermatofibrosarcoma protuberans – low-power magnification with diffuse infiltration of the skin and subcutaneous tissue (**A**: H&E); uniform and medium-sized spindle cells with a storiform or cartwheel pattern of growth (**B**: H&E 100×); minimal atypia and no mitotic figures or necrosis (**C**: H&E 400×); the cells have diffused strong staining for CD34 (**D**: immunohistochemistry 100×).

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Conflicts of interest

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Ethical considerations

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LETTER TO THE EDITOR

Dermatology societies in Africa: perspective from Angola

Sociedades de dermatologia em África: perspectiva de Angola

Lídia P. de Almeida Voumard[1], Laurinda Jamba-Calucango[2], Aurora E. Abel-Yara[3], and Juliano V. Isaías[4]*

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Dear Editor,

Fifty years after the country's independence, the Angolan Association of Dermatology and Venereology (AADV) was effectively instituted in Luanda on July 15th, 2025, opening a new page in the development of the discipline.

Dermatology is progressively emerging in Angola as a well-recognized medical specialty[1,2]: the Angolan College of Dermatology and Venereology was created in 2009 under the umbrella of the Medical Order, with a focus on the residency training program, ethics, deontology, and the suitability of dermatologists' professional qualifications; pending the creation of a professional society, the college was also assigned some functions typically performed by medical societies, such as continuing medical education.

AADV's mission is now to advance advocacy on skin and hair diseases, continuing education, clinical care, investigations, and to stimulate collaboration with other national and international societies, partner institutions, and industry.

Challenges faced by Sub-Saharan African (SSA) societies of dermatology

Despite their significant burden, there is low awareness of skin conditions among health workers and the general public. Weak surveillance systems further mask their true public health impact, and health workers have, in general, insufficient diagnostic capacity and access to treatment.

While simple skin conditions can often be managed by primary healthcare providers, such professionals are often unprepared to diagnose and treat less common skin, nail, mucous membrane, and hair diseases, resulting in significant delays and errors of diagnosis and treatment[2].

This situation is compounded by the low number of trained dermatologists (on average, circa de 1/400.000 pop.)[1] who are mostly concentrated in major cities, leaving poor-resource regions without the needed attention and care from trained professionals.

To counter-balance the limited access to quality skin care for many people living in rural and peri-urban areas, the working conditions and posting of trained dermatologists should be improved in order to enhance the capacity of the public health services.

Moreover, despite a growing interest in cosmetology, some key subspecialties, such as pediatric dermatology and histopathology, should be given particular attention to supplement standard clinical competencies[2].

Except for the Dermatology Society of South Africa, founded in 1946, most SSA dermatology societies, including the African Society of Dermatology and Venereology (ASDV)[3], are – if existing – still relatively young, with few members and limited resources to match their aspirations to advance skin health[4].

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In May 2025, the World Health Assembly unanimously approved a resolution on "Skin diseases as a global public health priority,"[5] which recognized the multiple challenges and key actions requiring urgent attention from member states and other stakeholders.

How AADV can advance skin health in Angola

The AADV can draw on its future members' expertise to organize clinical conferences and national days to mobilize, screen and respond to the needs of people with albinism, vitiligo and neglected tropical diseases[6], giving a voice to those suffering from stigma and discrimination.

Taking advantage of improved local internet services and the availability of new communication tools, the AADV can promote the use of digital technologies to enhance the capacity building of local personnel with the support of dermatologists.

The mobilization of incentives and support to promote epidemiological and clinical investigations is another AADV priority.

Angola was the first African Portuguese-speaking country (PALOP) to join the International League of Dermatology Societies (ILDS) in 2018 (Fig. 1)[6] and AADV members will be further encouraged to take advantage of the multiple presential and online events, courses, and other education materials offered by international societies such as the ILDS, International Foundation of Dermatology, ASDV, and the Ibero-Latin American College of Dermatology (CILAD).

During the 4th ASDV conference held in Tunis in 2024[3], which was attended by more than 600 dermatologists from 24 African countries, Angola was elected as the focal point for the PALOP dermatologists, which shall be encouraged to attend ASDV meetings to learn about the latest scientific and clinical research in Africa.

Last but not least, the strengthening of academic relationships with Brazilian and Portuguese institutions also offers great opportunities for continuing education. It is worth mentioning the support which was already granted to young Angolan dermatologists for postgraduate training (e.g., from the Unidade Local de Saúde Coimbra), as well as the support to participate in scientific conferences such as the Porto "Update on Dermatology treatments" international meetings[7]. Gracious access to the PJDV has been provided to Angolan dermatologists by the Sociedade Portuguesa de Dermatologia e Venereologia[7].

Figure 1. African ILDS members (*adapted from ILDS 2025 Members Map*[6]). ILDS: International League Of Dermatology Societies.

Conclusion

Dermatology in Angola and other SSA countries is facing multiple challenges, including high incidence and prevalence of skin diseases, lack of skilled dermatologists, weak laboratory infrastructure, and increasing costs of drugs. In Angola, the AADV can play a catalytic role for country-level coordinated action to improve continuing education, investigations, access to laboratory diagnostic capacities, and to essential medicines, integration with other programs, innovative service delivery models, epidemiologic surveillance, and general awareness on skin diseases.

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Conflicts of interest

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