

Adolescence Pseudolymphoma

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ABSTRACT

Objective: report an uncommon case of cutaneous pseudolymphoma in teenage years, undiagnosed for approximately 8 years old. **Methodology:** data were taken from medical records, patient interviews, photographic records of the injuries, diagnostic methods, and literature review. The paper was subjected and approved by the Research Ethics Committee (REC), under the number 4.952.193, authorized by the patient and their legal sponsor. **Final Conclusions:** the related case shows the importance of reliable and differential diagnoses since the patient carried the injury through approximately eight years without getting any diagnosis and/or treatment. Furthermore, the unusual age and the location of the injuries make the information presented here fundamental to helping other professionals and contributing to the Public Health System.

Keywords: Pseudolymphoma, Non-Hodgkin's Lymphoma, Differential diagnosis, Teenager health

INTRODUCTION/JUSTIFICATION

The lymphomas represent a group of malignant neoplasms with its origin from lymphoid cells; they are presented as solid tumor masses and originate from lymphoid tissues, such as lymph nodes. They are divided into two main groups: Non-Hodgkin's Lymphoma (NHL) and Hodgkin Lymphoma, or Hodgkin disease (HD).¹ About 30% of Non-Hodgkin's Lymphoma affect extranodal tissues, like skin, the second most involved organ after the gastrointestinal tract.² They are considered indolent, but they are also a disease for which the cure has not been found yet.³

The pseudolymphomas, on the other hand, are a heterogenous group of benign cutaneous lymphoproliferative reactions constituted by B and T cells.⁴ Another name given to these reactions is cutaneous lymphoid hyperplasia, a better description of its benign path. In this context, there are cutaneous sarcomatosis, cutaneous lymphocytoma, benign cutaneous lymphadenosis, Spiegler and Fendt pseudolymphoma and actinic reticuloid as other accepted terminologies to describe this dermatosis.⁵

It is proposed that pseudolymphomas are an inflammatory response that generates an accumulation of inflammatory cells due to several stimuli,

and the result of this inflammatory response, evidenced by histology, is a cutaneous manifestation like that of lymphomas, consisting of nodules, papules, and macules, generating diagnostic doubt.^{6,7}

Regarding epidemiology, both pseudolymphoma and lymphoma are observed mostly in adults, being more common in women than in men, in a ratio of 2:1. It mainly affects young adults, with an average age of 34 years. As for location, there is a preference for involvement in the head, neck, and extremities.^{7,8} Unlike the pseudolymphoma, lymphoma has a variable location.

Therefore, it is relevant to report the case of a patient with cutaneous pseudolymphoma, given its scarcity in the literature, mainly because its location and age range differ from what is usually found, aiming to add information that might help other professionals to form the diagnosis of this pathology and attest to the need for a differential diagnosis with Lymphoma, mainly because of its reserved prognosis. Therefore, the need for an early and assertive diagnosis is emphasized, which provides the patient with the possibility of initial intervention, the moment when treatment is, in most cases, more effective. In addition, the generalized benefit of this for the Public Health System is evident, guaranteeing the completeness and quality of life.

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CASE REPORT

Patient, female, 11 years, white, with no pathological antecedents, attended the Specialty Medical Ambulatory of the State of São Paulo, complaining about a skin injury on her right thigh since the age of three.



Figure 1: Reddish macula in the region of the right thigh



Figure 2: Reddish macula in the region of the right thigh - flash

The wound started as a reddish macule, progressing to a hypertrophic lesion measuring about 2 cm in length and 1 cm in thickness, denying itching at the time of consultation, although it has been reported intermittent local itching and occasional bleeding, local pain and size increasing were denied.

The patient claims to have had a pediatric consultation in the Public Health System as soon

as the lesions appeared, on occasions where the conduct was merely expectant, without conducting tests, drug prescriptions, or referral to a dermatologist specialist. Just after 7 years, medical care was demanded again due to the evolution of the injury. At that time, a consultation was held with another pediatrician from the Public Health System, with a referral to a dermatologist specialist for diagnosis, treatment, and attendance, with a response delay of approximately 45 days, as described in this case report. Among the initial diagnostic hypotheses, lymphoproliferative lesions were listed, with emphasis on cutaneous B-cell and T-cell lymphoma, hemangioma, and hypertrophic scar. Other options would be contact dermatitis, drug eruptions actinic reticuloid, and syphilis.

The initial procedure instituted was a biopsy of the lesion, an elliptical skin fragment measuring 2.8x1.5 centimeters in area and 0.8 centimeters thick, covering the subcutaneous tissue, fixed in formalin. Material sent for histopathology, with the conclusion showing skin with dense lymphoid infiltrate in the dermis, heterogeneous, with germinal center and focally dilated lymphatic vessels in the superficial dermis, free surgical margins, being subsequently forwarded for immunohistochemical study and diagnostic opinion, and the results obtained are described in Table 1.

Table 1

Immunohistochemical panel

Antibody	Results
CD20 - B lymphocyte antigen	Positive
CD3 - T lymphocyte receptor (epsilon chain)	Positive
CD4 - auxiliaries T cell antigen	Positive
CD8 - cytotoxic T cell antigen	Positive
CD30- ki-1 antigen	Negative
CD7, T lymphocyte, NK cells and thymocyte, CD7-272 clone	Positive
Deoxynucleotidyl transferase (TdT)	Negative
CD10 - common antigen of acute lymphocytic leukemia (CALLA)	Negative
BCL-2 anti-apoptotic protein	Negative
BCL6 protein - transcription factor (zinc finger)	Positive

Source: The Authors

From the immunohistochemical study, it was possible to obtain the confirmatory diagnosis, showing skin being infiltrated by dense lymphocytic infiltrate in the superficial and middle dermis, in a strip, without atypia, with a nodular infiltrate. Presence of occasional plasmacytes intermingled. Predominance of population T (CD3+), with the usual CD4:CD8 ratio, followed by population B (CD20+). The findings correspond to reactive lymphoid hyperplasia (cutaneous pseudolymphoma).

No drug treatment was instituted because there was no need since diagnostic and therapeutic excision of the lesion was performed.



Figure 3: Lesion after exeresis in the right thigh

As for the patient's medical release guidelines, a vigilant look was advised on the wound scar and any similar injuries that may appear on the rest of the body, and if changes are noticed, immediate return is necessary.

After approximately three years since the exeresis, the patient reports a good evolution of the healing and denies the appearance of similar injuries.

DISCUSSION

Pseudolymphoma is not a specific disease but an inflammatory response to unknown stimuli that generate an accumulation of inflammatory

cells, as observed in the reported case – which, by the way, represents the majority of cases –, or even to already known stimuli, whose possible causes were already covered in the literature: contact dermatitis; lichenoid pigmented purpuric dermatosis; sclerosus and atrophic lichen; secondary syphilis; morphea inflammatory state; nodular scabies; lupus panniculitis; viral resistant (herpes simplex/zoster, molluscum contagiosum); tattoos; vaccinations; trauma; jewelry for pierced ears, as well as gold; acupuncture; with *Borrelia burgdorferi* or *Leishmania* and reactions to drugs (anticonvulsants, antipsychotics, antihypertensives, cytotoxics, antirheumatics, antibiotics, anxiolytics, antihistamines, antiarrhythmics, sex steroids, agents that transmit lipids, TNF alpha agents, cyclosporine and tocilizumab).^{4,5}

As for the pathophysiology of pseudolymphoma, Hussein⁸ suggests that the result of cutaneous pseudolymphomas occurs from predominantly dermal recruitment and selective accumulation of one or two subsets of immune cells (B and T cells) through sequential stages. Initially antigenic, the encounter involves interactions between epidermal Langerhans cells, extraneous antigens, and neighboring keratinocytes, leading to the generation of antigenic signals that are triggered by immunocompetent B and T lymphocytes, macrophages, and dermal dendritic cells. Dermal lymphocytes, histiocytes, and dendritic cells leave capillaries in the papillary dermis, pass through the epidermis as intraepithelial lymphocytes, and leave the skin via afferent lymphatic vessels.

Along the way, these cells positively regulate their immunocompetence with the release of several mediators (cytokines, chemokines, cell adhesion molecules, and other mediators), which help in the selection, recruitment, extravasation, and migration of immune cells (lymphocytes, histiocytes, and dendritic cells) through the connective tissue to specific skin compartments. They also stimulate dermal fibroblasts and the endothelial cell lining and dermal vessels to participate in the ongoing inflammatory process. The tissue-specific location and accumulation of immune cells would, therefore, result in the formation of cutaneous pseudolymphoma cells.

The result of this inflammatory response is a clinical manifestation similar to what occurs in

lymphomas, manifest as solitary nodules, papules, and infiltrative plaques resulting from lymphocytic infiltration, generating, then, the diagnostic doubt. Less frequently, they may present as persistent erythema or exfoliative erythroderma. Furthermore, although there is no unique clinical picture that proves a malignant or benign lesion, multiple nodules or plaques support the suspicion of a malignant lymphoma. Lymphadenopathy is also more suggestive of lymphoma. However, the mixed type of B- and T-cell pseudolymphoma can also show lymphadenopathy.⁵

As for the adopted conduct, occasionally, such similarity requires multiple biopsies, immunohistochemical evaluation, and molecular biology techniques, and the existence of a single cell type points to the lymphoma, while polyclonality points to pseudolymphoma. This differentiation needs to be emphasized, considering the patient's treatment and prognosis.^{4,9}

Diagnostic confirmation, therefore, is made by a combination of clinical signs, histopathology, immunohistochemistry, and patient follow-up to analyze the course of the disease.⁵ The main histological features that support the diagnosis of pseudolymphoma are the presence of a mixed infiltrate with histiocytes, eosinophils, lymphocytes, and plasma cells. The presence of macrophages with tingible bodies, preserved and evenly spaced follicular dendritic cells (highlighted by CD21 immunohistochemical staining), preserved polarized germinal centers, and absence of BCL-2 staining favor the diagnosis of pseudolymphoma. Thus, the need for immunohistochemistry to carry out the differential diagnosis has become evident. In addition, the clinic and follow-up are essential for definitive treatment.⁶

Treatment options for pseudolymphoma include observation, topical agents – such as potent steroids and intralesional corticosteroids –, systemic agents, and physical modalities – such as cryosurgery, photochemotherapy, local radiotherapy, and surgical excision, which was adopted in the described report. In Miguel's systematic review⁵, it was shown that the choice of treatment must be made individually for each patient according to the etiology and location of the wound. Due to the possible evolution to malignant lymphoma that may occur, perhaps induced by persistent antigenic

stimulation, a follow-up of at least five years is necessary to rule out the risk of cutaneous lymphoma and, if any surgical excision is performed, a vigilant follow-up is highly recommended. However, progression to cutaneous lymphoma was observed in a minority of cases.^{5,10,11}

In the study by Hussein⁸, a histopathological model was described that suggests the potential pathological pathway for the development of cutaneous lymphoma from an atypical proliferation and pseudolymphoma. Cutaneous lymphomagenesis can go through three stages. In the first, persistent antigenic stimulation of lymphoid tissues associated with the skin leads to the formation of lymphoid infiltrates (analogous to reactive lymph nodes), that is, cutaneous pseudolymphomas. During this first stage, the host's immune system manages to control the lymphoid proliferation, there are no genetic alterations; therefore, the lesions have a benign biological behavior. In the second phase, with tissue damage already occurring, rare cutaneous pseudolymphomas acquire some genetic alterations and evolve into atypical lymphoid proliferations. In this phase, the host's immune system begins to lose control over the lymphoid proliferations and the lesions have an unpredictable biological behavior. These atypical lesions may regress, persist, or progress to lymphomas. In the third stage, there is the occurrence of significant genetic changes that push these atypical lesions on the path to lymphomatous transformation. During the third phase, the host's immune system loses control over the lymphoid proliferations, and the lesions show aggressive behavior.

CONCLUSION

Therefore, the importance of adequate medical care and previous theoretical-clinical knowledge is evident since pseudolymphoma and B- and T-cell lymphoma are pathologies with similar clinical and/or histological presentation, with totally different prognoses, for an assertive diagnosis and consequent appropriate treatment. Furthermore, the need for prior understanding of the natural history of the disease is emphasized, given the possible, but rare, progression of pseudolymphoma to cutaneous lymphoma.

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Editor:
Prof. Dr. Felipe Villela Gomes

Received: mar 23, 2022
Approved: mar 06, 2023
