Actas Dermosifiliogr. 2016;xxx(xx):xxx–xxx

ACTAS Dermo-Sifiliográficas

Full English text available at www.actasdermo.org

REVIEW

Cutaneous Pseudolymphomas☆

D. Romero-Pérez, M. Blanes Martínez,* B. Encabo-Durán

Servicio de Dermatología, Hospital General Universitario de Alicante, Alicante, Spain

Received 21 December 2015; accepted 1 May 2016

KEYWORDS
Pseudolymphoma;
Skin;
Cutaneous lymphoid hyperplasia

Abstract The term *cutaneous pseudolymphoma* refers to benign reactive lymphoid proliferations in the skin that simulate cutaneous lymphomas. It is a purely descriptive term that encompasses various reactive conditions with a varied etiology, pathogenesis, clinical presentation, histology, and behavior. We present a review of the different types of cutaneous pseudolymphoma. To reach a correct diagnosis, it is necessary to contrast clinical, histologic, immunophenotypic, and molecular findings. Even with these data, in some cases only the clinical course will confirm the diagnosis, making follow-up essential.

PALABRAS CLAVE
Pseudolinfoma;
Piel;
Hiperplasia linfoide cutánea

Pseudolinfomas cutáneos

Resumen El término pseudolinfoma cutáneo designa proliferaciones linfoides cutáneas benignas de naturaleza reactiva que simulan linfomas cutáneos. Se trata de un término puramente descriptivo que engloba diferentes entidades reactivas, con diversa etiología, patogénesis, presentación clínica, histología y comportamiento. En el presente artículo revisaremos los distintos tipos de pseudolinfoma cutáneo. Como veremos, para llegar al correcto diagnóstico de los mismos será preciso en cada caso la integración de los datos clínicos con los histopatológicos, inmunofenotípicos y moleculares. Incluso entonces, en ocasiones solo la evolución confirmará el diagnóstico, por lo que el seguimiento será esencial.

Introduction

Cutaneous pseudolymphomas are benign reactive lymphoid proliferations that simulate cutaneous lymphomas clinically, histologically, or both clinically and histologically.[1–6] The concept was described for the first time in 1891 by Kaposi under the name *sarcomatosis cutis*. Since

☆ Please cite this article as: Romero-Pérez D, Blanes Martínez M, Encabo-Durán B. Pseudolinfomas cutáneos. Actas Dermosifiliogr. 2016. http://dx.doi.org/10.1016/j.ad.2016.05.003

* Corresponding author.
E-mail address: blanes_marmar@gva.es (M. Blanes Martínez).

then, these proliferations have received many names and the initial descriptions all corresponded to B-cell pseudolymphoma.[4,5,7,8]

Traditionally, cutaneous pseudolymphomas have been classified according to their histologic and immunophenotypic characteristics or rather in relation to the lymphoma they simulate. In other words, they are categorized as cutaneous B-cell pseudolymphomas or cutaneous T-cell pseudolymphomas, depending on the predominant lymphocytic component.[9] While the distinction is frequently artificial, this classification system is still the widely used system for categorizing pseudolymphomas.

The list of cutaneous pseudolymphomas has grown in recent years with the inclusion of multiple reactive conditions with histopathologic features mimicking those of true lymphomas. It is also noteworthy that several entities that were originally considered to be cutaneous pseudolymphomas have since been reclassified as low-grade lymphomas based on clinical and pathologic findings, molecular biology studies, and follow-up data.[6]

Epidemiological data on cutaneous pseudolymphomas are scarce, although B-cell pseudolymphomas appear to be more common than their T-cell counterparts, and they are also more common in female patients.[4,5,10] Cutaneous pseudolymphoma generally affects adults, although it can occur at any age. No familial cases have been reported.[3]

The proliferation of skin-associated lymphoid tissue (SALT), the cutaneous analog of mucosa-associated lymphoid tissue (MALT), following antigenic stimulation has been proposed as a contributory factor in the pathogenesis of cutaneous pseudolymphoma .[11] Accordingly, cutaneous pseudolymphoma could potentially progress to a true cutaneous lymphoma with permanent antigenic stimulation, as occurs in the gastric mucosa in the presence of persistent *Helicobacter pylori* infection.[12] However, while there have been some reports of progression to cutaneous lymphoma,[13–17] true progression from a correctly diagnosed pseudolymphoma is very rare, if not impossible.

To diagnose cutaneous pseudolymphoma it is necessary to contrast clinical and histologic findings, with assessment of the architecture and composition of the inflammatory infiltrate, and to complement these findings with immunohistochemistry and gene rearrangement studies.[6,18,19] These clonality studies generally reveal a polyclonal pattern. Nevertheless, it is not always possible to demonstrate clonality in true lymphomas, and certain pseudolymphomas have monoclonal B-cell and T-cell populations.[5,8,20–26] Accordingly, although gene arrangement studies are useful, their results must be interpreted with caution and within the context of the data available.

In the rest of this paper we will describe the main types of cutaneous pseudolymphoma (Table 1).

Table 1 Cutaneous Pseudolymphoma.

Lupus erythematosus panniculitis
Pseudolymphoma in tattoos
Pseudolymphoma at the site of vaccination
Lymphocytoma cutis
Pseudolymphoma in acrodermatitis chronica atrophicans lesions
Pseudolymphomatous folliculitis
Lymphomatoid drug reaction
Morphea
Acral pseudolymphomatous angiokeratoma
T cell–rich angiomatoid polypoid pseudolymphoma
Pretibial lymphoplasmacytic plaque
Secondary syphilis
Persistent arthropod bite reaction
Actinic reticuloid
Lichen sclerosus et atrophicus
Lichen aureus
Solitary T-cell pseudolymphoma
Lichenoid keratosis
Lymphomatoid contact dermatitis
Atypical lymphoid proliferation in patients with human immunodeficiency virus
$CD30^+$ pseudolymphomas
Immunoglobulin G4-related disease
Annular lichenoid dermatitis
Palpable migratory arciform erythema
Other cutaneous pseudolymphomas

Lupus Erythematosus Panniculitis

Lupus with subcutaneous involvement, a condition known as lupus erythematosus panniculitis, can raise clinical and particularly histologic suspicions of panniculitis-like T-cell lymphoma.[6,27]

Lupus erythematosus panniculitis presents as plaques or subcutaneous nodules in areas rarely affected by other forms of panniculitis, such as the face, the shoulders, and the proximal aspect of the arms. Antinuclear antibodies and other diagnostic criteria for systemic lupus erythematosus may be absent.

Histologic examination shows a predominantly lobular panniculitis with dense lymphoid infiltrates in the deep dermis and the hypodermis, along with wide fibrous septae on occasions. The infiltrate is mixed, with abundant B cells, plasma cells, and clusters of plasmacytoid dendritic cells, frequently forming reactive germinal centers. The dermal-epidermal junction may show the characteristic interface dermatitis associated with the underlying connective tissue disease, and this is a key finding for the differential diagnosis. In lupus erythematosus panniculitis, unlike in panniculitis-like T-cell lymphoma, histology does not show cytophagocytosis or adipocyte rimming (atypical lymphoid cells surrounding the adipocytes). T-cell receptor (*TCR*) gene rearrangement will show a polyclonal pattern.[6,27]

Histologic features of panniculitis-like T-cell lymphoma and lupus erythematosus panniculitis may, albeit rarely, overlap. In one study of 83 patients with panniculitis-like T-cell lymphoma, Willemze et al.[28] observed abundant plasma cells interspersed with $CD4^+$ T cells in 4 patients who also had lupus erythematosus, leading to an initial misdiagnosis of lupus erythematous panniculitis. The presence of cellular atypia together with a loss of pan-T-cell markers and/or clonal TCR-γ rearrangement was key to establishing a correct diagnosis.[28]