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A review of 55 cases of cutaneous lymphoid hyperplasia: reassessment of the histopathologic findings leading to reclassification of 4 lesions as cutaneous marginal zone lymphoma and 19 as pseudolymphomatous folliculitis

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Summary To clarify the confusion surrounding the diagnosis of cutaneous lymphoid hyperplasia (CLH) that was formerly described as lymphadenosis benigna cutis, lymphocytoma cutis, or lymphocytic infiltration of Jessner and to assess whether newly recognized diagnoses, such as cutaneous marginal zone lymphoma and pseudolymphomatous folliculitis (PLF), may have been overlooked, we reexamined 55 Japanese cases of nonepidermotropic lymphoproliferative disorder that had previously been diagnosed as "cutaneous pseudolymphoma." In all these cases, the immunohistochemical expressions of CD1a, CD3, CD4, CD8, CD20, CD21, CD30, CD43, CD56, CD68, CD79a, κ and λ chains, S-100 protein, and latent membrane protein were assessed. In addition, in 13 cases the gene rearrangement of the immunoglobulin heavy chain was investigated using a polymerase chain reaction method. As a result of these investigations, we have identified 4 cases of cutaneous marginal zone lymphoma, 19 cases of PLF, 1 case of diffuse large B-cell lymphoma, and 2 cases of solitary nonepidermotropic pseudo–T-cell lymphoma, with the remaining 29 cases being CLH. Cutaneous marginal zone lymphoma, which represented 7.3% of the total, was distinguished from CLH by the presence of patchy or diffuse proliferation of centrocyte-like cells, plasma cells at the periphery of the lymphocytic infiltration, monotypic restriction of the light chains, and gene rearrangement of the immunoglobulin heavy chain. Pseudolymphomatous folliculitis was identified by the presence of activated pilosebaceous units with abundant CD1a-and S-100 protein–positive T-cell–activated dendritic cells. Of the cases that were reassessed, 34.5% were PLF.

1. Introduction

The term *cutaneous pseudolymphoma* is given to a group of disorders with lymphocytic infiltration that histologically resembles cutaneous lymphoma. Although these conditions were formerly known as lymphadenosis benigna cutis, including synonyms such as lymphocytoma cutis, pseudo-

Abbreviations: CMZL, Cutaneous marginal zone lymphoma; PLF, Pseudolymphomatous folliculitis; CLH, Cutaneous lymphoid hyperplasia; IgH, Immunoglobulin heavy chain; PCR, Polymerase chain reaction; DLBL, Diffuse large B-cell lymphoma.

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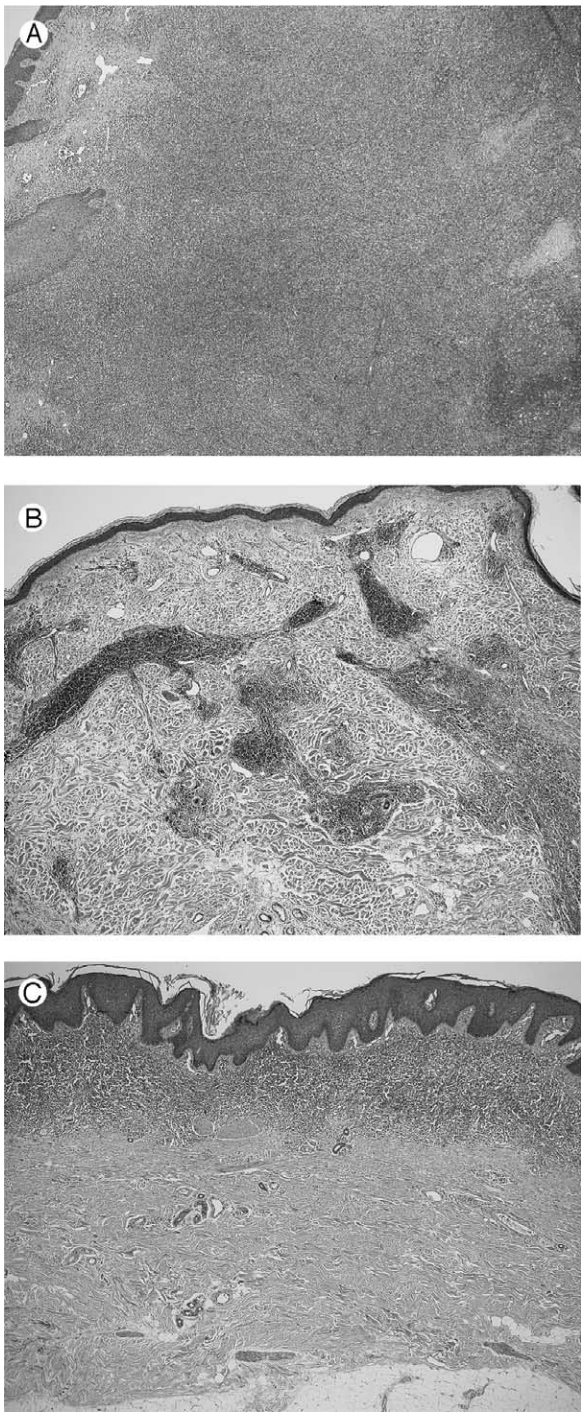

Fig. 1 Three histologic patterns of cutaneous lymphoid infiltration. Diffuse pattern (A), patchy pattern (B), and band-like pattern (C).

lymphoma of Spiegler-Fendt or cutaneous lymphoplasia, and lymphocytic infiltration of Jessner, the term *cutaneous lymphoid hyperplasia* (CLH) is currently the recommended term [1,2]. In particular, there are various opinions about whether lymphocytic infiltration of Jessner is a distinct entity [3]. In CLH, there is no epidermotropism in the Grenz zone and there is dense lymphocytic infiltration throughout the skin layers from the dermis to the subcutis. The infiltrating cells are mainly mature lymphocytes and there are multiple lymphoid follicles. Both plasma cells and scattered eosinophils are present. A variant with marked plasma cells has been reported [4].

Recently, it has been suggested that lesions that are really cutaneous marginal zone lymphoma (CMZL) may have been erroneously diagnosed as CLH [1,2,5]. Both CMZL and cutaneous follicular lymphoma are uncommon in the Japanese population [6]. However, grouping these diseases under the CLH diagnostic label may be misleading because both these diseases are curable through simple resection in the early stages and carry an excellent prognosis, with the 5-year survival being 95% for CMZL and 98% for cutaneous follicular lymphoma [7,8].

In addition, before the establishment of pseudolymphomatous folliculitis (PLF) as a separate diagnosis within the cutaneous pseudolymphoma group, PLF used to be classified as a form of CLH [9]. In the present study we have reclassified the nonepidermotropic types of cutaneous pseudolymphomas based on the recently changed criteria.

2. Patients and methods

A retrospective review of cases identified 55 patients who were treated between 1990 and 2001 for cutaneous pseudolymphomas without epidermotropism. Of these 55 cases, 30 had been diagnosed at Saitama Medical School and 25 after further consultation. All the pathological material that was reviewed had been obtained at the initial

Table 1 The antibodies used in this study

Antigen	Clone	Manufacturer (location)	Dilution
CD1a	010	Immunotech (Marseille, France)	×1
CD3	PS1	Novocastra (Newcastle, UK)	×100
CD4	1F6	Novocastra	×40
CD8	C8/144B	Dakopatts (Glostrup, Denmark)	×100
CD20	L26	Dakopatts	×100
CD21	1F8	Dakopatts	×100
CD30	BerH2	Dakopatts	×40
CD43	DF-T1	Dakopatts	×25
CD56	1B6	Novocastra	×50
CD68	KP-1	Dakopatts	×40
CD68	PG-M1	Dakopatts	×200
CD79a	JCB117	Dakopatts	×100
κ	A8B5	Dakopatts	×100
λ	C4	Immunotech	×50
S-100 protein	(Polyclonal)	Dakopatts	×300
LMP-1	CS1-4	Dakopatts	×40

Abbreviation. LMP-1, latent membrane protein-1.