QUIZ SECTION

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A Red Domical Nodule on the Nose: A Quiz

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A 60-year-old male patient presented to our department with a 2-month history of nasal rash. The patient had experienced recurrent folliculitis-like papules and papulopustules in the same location for the past 2 years. Initially, the rash subsided after using topical iodophor and mupirocin topical, but it had recurred in the past 2 months. Despite repeating the same above-mentioned treatments, the rash did not subside and instead increased in size over time. The patient was in good overall health and did not exhibit any accompanying systemic symptoms. There was no history of insect bites, prolonged sun exposure, or trauma prior to the lesion. Systematic examination did not reveal any superficial lymph node enlargement or other abnormalities. A red domical nodular lesion, roughly 1.5 cm in diameter, was observed on the nose's dorsum. The lesion had defined edges, a firm texture, and appeared smooth (Fig. 1A).

Histopathological examination of the biopsy specimen revealed slight atrophy of the epidermis, distorted, hyperplastic hair follicles were observed in the dermis, and dilated, activated pilosebaceous units were surrounded by dense lymphocytes. (Fig. 2A, B). Immunohistochemical staining (Fig. 3A–G).

Two months after the rash biopsy, the patient's skin lesion resolved spontaneously without any additional specific treatment. (Fig. 1B).

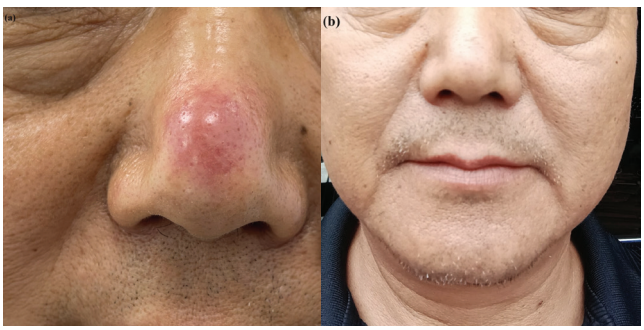

Fig. 1. (A) Clinical picture: red, domical nodule on the nose. (B) Follow-up picture: the rash disappeared. The patient gave consent for his photographs and medical information to be published in print and online and with the understanding that this information may be publicly available.

What is your diagnosis?

Differential diagnosis 1: Cutaneous marginal zone lymphoma

Differential diagnosis 2: Small and medium-sized pleomorphic cutaneous T-cell lymphoma

Differential diagnosis 3: Follicular mycosis fungoides

Differential diagnosis 4: Other cutaneous pseudolymphomas

See next page for answer.

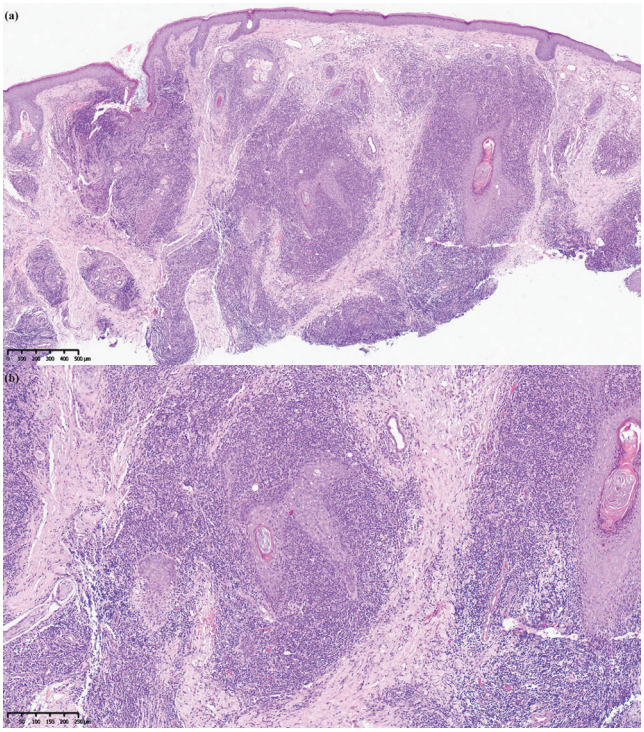

Fig. 2. Haematoxylin-eosin staining. (A) Original magnification x 50. (B) Original magnification x 100. Histopathology: slight atrophy of the epidermis, distorted, hyperplastic hair follicles were observed in the dermis, and dilated, activated pilosebaceous units were surrounded by dense lymphocytes. The majority of infiltrating cells were lymphocytes and some histiocytes, which invaded the hair follicle epithelium and disrupted the structure of the hair follicle. The infiltrate and the epidermis were separated by a Grenz zone, and the infiltrated cells exhibited relatively uniform morphology and size.

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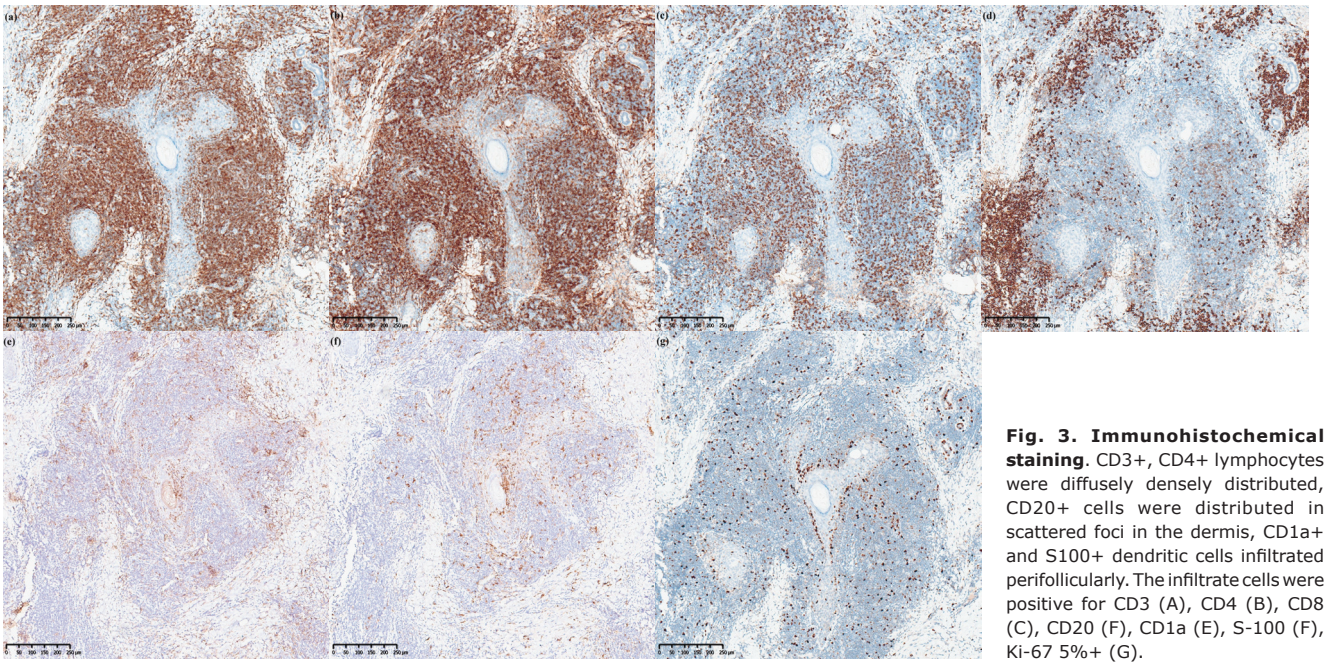

Fig. 3. Immunohistochemical staining. CD3+, CD4+ lymphocytes were diffusely densely distributed, CD20+ cells were distributed in scattered foci in the dermis, CD1a+ and S100+ dendritic cells infiltrated perifollicularly. The infiltrate cells were positive for CD3 (A), CD4 (B), CD8 (C), CD20 (F), CD1a (E), S-100 (F), Ki-67 5%+ (G).

ANSWERS TO QUIZ

A Red Domical Nodule on the Nose: A Commentary

Acta Derm Venereol 2024; 104: adv41199.
DOI: 10.2340/actadv.v104.41199

Diagnosis: **Pseudolymphomatous folliculitis**

Pseudolymphomatous folliculitis(PLF) is an uncommon skin disorder characterized by lymphoid hyperplasia. It was first clearly identified as a variant of pseudolymphoma 1986 (1). PLF affects individuals of all ages and does not show a clear gender predisposition (2). Typically, the lesions are located on the face, particularly on the nose, cheeks, and forehead. Rashes on the scalp and trunk are infrequently observed. The common clinical manifestation of PLF is the presence of red or purplish domical nodules (3–6). While most cases are asymptomatic, some patients may experience mild itchiness or pain (2). Single lesions are common, while multiple lesions are infrequent (7, 8).

The aetiology of PLF is unknown. The dense distribution of CD1a/S100$^+$ perifollicular dendritic cells has been recognized as an essential characteristic of PLF (3, 9). As is known, dendritic cells, which are specialized antigen-presenting cells in the body, have the ability to efficiently take up and process foreign antigens and subsequently deliver them to T lymphocytes. The significantly increased number of CD1a+ dendritic cells in all follicular segments of PLF suggests that there may be underlying antigenic stimulus residues in the follicle that cause an increase in dendritic cells and thus recruitment of T cells. PLF may be a result of a delayed reaction to antigens situated in the epithelium or follicular lumen, which is supported by the spontaneous regression of PLF after biopsy, as the so-called implied antigens are removed (1, 3). However, the reasons for the antigenic challenge have not been explored and the exact pathogenesis of this disease remains obscure. In our case, the patient had a 2-year history of recurrent localized folliculitis, and this exogenous stimulus may have been involved in the development of PLF (10).

The clinical characteristics of pseudolymphomatous folliculitis are atypical, and the diagnosis relies on histopathological and immunohistochemical analysis.

The pathological feature of pseudolymphomatous folliculitis is nodular dense or diffuse infiltration of lymphocytes extending from the dermis to the subdermis. The infiltrate is separated from the epidermis by the Grenz zone (2, 5). Distorted and hyperplastic hair follicles are seen in the dermis, surrounded by dilated and activated pilosebaceous units encircled by dense lymphocytes, leading to deformation of the follicle wall. Follicular invasion can be classified into 2 types: the first where hair follicles are destroyed and eventually disappear, and the other where the hair follicles are not damaged but become activated, resulting in irregular enlargement of the follicle wall (2, 4, 7, 11, 12). In our case, we observed distorted and hyperplastic hair follicles surrounded by lymphocyte infiltration with some cells invading the hair follicle epithelium, causing damage to the follicle wall. Immunohistochemistry revealed a mixture of CD3, CD4 positive T lymphocytes and CD20 positive B lymphocytes (2, 3, 5). Many dendritic cells with positive expression of CD1a protein and S100 protein were also seen in and around the pilosebaceous units. This is a distinctive histological feature of PLF, but not a diagnostic sign of cutaneous lymphomas (11).

The rarity and atypical clinical manifestations of PLF warrant consideration of multiple differential diagnoses including Rosacea, follicular lymphomatoid papulosis, and lymphoma (13). Rosacea shares similarities with PLF in the presence of surrounding pilosebaceous units accompanied by lymphocytic infiltration. However, distinguishing features include the absence of significant CD1a/S100+ dendritic cell proliferation in Rosacea, by which it can be distinguished from PLF (4,13). Follicular lymphomatoid papulosis, on the other hand, is characterized by immunohistochemical features such as proliferation of CD3$^+$, CD4$^+$, and CD30$^+$ lymphocytes, with CD8 typically being negative. This feature makes possible differentiation from PLF (13, 14).

PLF is a challenging condition to diagnose due to the presence of atypical lymphocytes that can mimic primary cutaneous malignant lymphomas. These include cutaneous marginal zone lymphoma, small- and medium-sized pleomorphic cutaneous T-cell lymphoma, follicular mycosis fungoides, and other cutaneous pseudolymphomas. However, PLF can be distinguished from other types of cutaneous lymphoma by its distinct histopathological and immunohistochemical features.

In most malignant lymphomas, except for follicular mycosis fungoides, the pilosebaceous units are usually typically destroyed or absent. Marginal zone lymphoma can be separated from PLF by the diffuse proliferation of marginal zone cells, often forming sheets or zones of monotonous plasma cells, along with the existence of reactive lymphoid follicles (9, 10, 13). Additionally, features such as facial predisposition and solitary lesions aid in distinguishing PLF from pleomorphic small-/medium-sized T-cell lymphoma (3). The lack of a heterogeneous epidermal infiltrate of atypical cells is also in PLF a distinguishing factor between PLF and follicular mycosis fungoides (6, 12, 13).

The primary treatment for PLF is skin biopsy. In many cases of isolated lesions, the rash has been observed to resolve spontaneously after biopsy (6). Corticosteroid injections are recommended if the rash is incompletely excised (12). Additionally, antimalarial drugs, methotrexate, cyclosporine, triamcinolone, and tacrolimus may be considered as therapeutic options for residual lesions after biopsy or multiple lesions (3, 5, 7, 12, 13).

Although there have been no reports of PLF progressing to a malignant lesion, there is a possibility of spontaneous recurrence. Therefore, some authors recommend a follow-up period of 6 months after biopsy and to monitor the recovery of the rash (15).

In this particular case, the residual rash had resolved on its own without any other further treatment, 2 months after biopsy. We conducted a 6-month follow-up, and observed no recurrence of the lesion.

The authors have no conflicts of interest to declare.

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