Cutaneous pseudolymphoma of the breast

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Cutaneous pseudolymphoma (PL) refers to a reactive T or B- cell proliferative disorder in reaction to some known or unknown stimuli. The most common site of involvement of pseudolymphoma is the face followed by the scalp. Because of its similarity with true lymphoma in both clinical and pathological aspects, differentiating between them is often difficult but fundamental due to their completely different prognoses and treatments. We report a case of cutaneous pseudolymphoma of the breast in association with fibrocystic change of the breast, and a long history of taking hormonal drugs, in a 35-year-old woman. There was a very good response to intralesional steroid injections and oral hydroxychloroquine.

Keywords: breast, lymphoma, pseudolymphoma

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INTRUDUCTION

Cutaneous pseudolymphoma was first described by Kaposi (1891) as sarcomatosis cutis, and was then modified to the current term cutaneous lymphoid hyperplasia. It refers to a reactive T or B cell proliferative disorder in reaction to some known or unknown stimuli [1,2].

The most common site of involvement of pseudolymphoma (PL) is the face followed by the scalp [3]. Because of its similarity with true lymphoma in both clinical and pathological aspects, differentiating between them is often difficult but fundamental due to their completely different prognoses and treatments. Here, we report a case of cutaneous pseudolymphoma of the breast in association with fibrocystic change of the breast, and a long history of taking hormonal drugs.

CASE REPORT

A 35-year-old woman was referred to our dermatology clinic with chronic periareolar erythematous plaques. Lesions had appeared 6 months ago as two asymptomatic small erythematous patches which grew gradually over 6 months.

Neither topical corticosteroid nor oral antihistamines prescribed at another hospital had been effective. There was no history of recent insect bite or vaccination, but she had received hormonal drugs after in vitro fertilization (because of her husband's infertility) including GnRH agonist, FSH, LH, progesterone in addition to heparin, folic acid and aspirin. However, she had discontinued all the medications one month before lesions appeared.

Physical examination revealed an erythematous horseshoe shaped plaque with several periareolar small plaques on the left breast with an indurated base without excoriation or discharge (Figure1). She had no palpable axillary lymph nodes. Breast examination revealed multiple masses in both breasts which were compatible with fibrocystic change on ultrasound, and confirmed by aspiration. Review of systems was negative for any systemic symptoms such as fever, weight loss, and night sweats. Routine laboratory investigations and chest X- ray revealed no abnormality.

Biopsy of the cutaneous lesion showed unremarkable epidermis. The underlying dermis revealed a very narrow zone of uninvolved

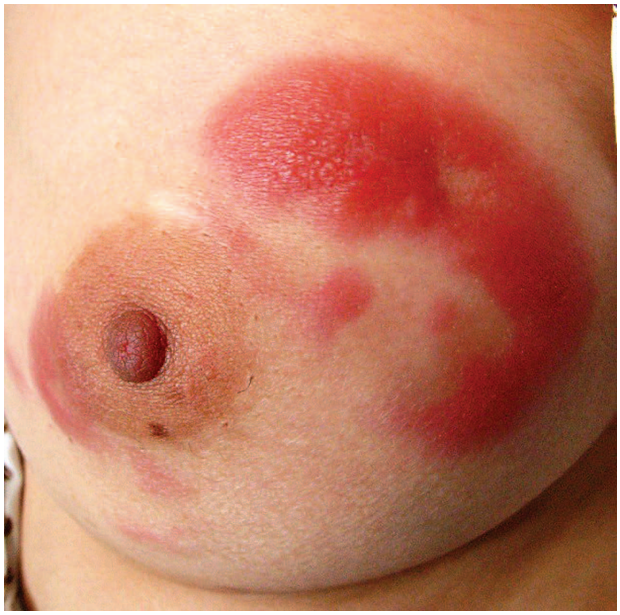

Figure 1. Erythematous horseshoe shaped plaque with several periareolar small plaques on the left breast with an indurated base without excoriation or discharge

normal connective tissue (resembling Grenz zone), and a dense infiltrate of lymphocytes and some histiocytes, plasma cells and rare eosinophils in reticular and deep dermis. The infiltration was also extended down to hypodermis and produced prominent germinal centers in multiple foci (Figure 2). Phenotypic analysis showed that most of the lymphocytes were CD20 positive (Figure 3) while some were CD3 positive but they were negative for CD56 and CD10. Bcl2 was positive in most lymphoid cells while ki67 was positive in 10% of the cells. Monoclonal rearrangement of T-cell receptor gamma, using multiplex PCR technique, was negative for clonality. These findings were compatible with B cell pseudolymphoma or cutaneous lymphoid hyperplasia. Serological tests for Borrelia Burgdorferi were negative.

We tried cryotherapy on one side and intaleisional corticosteroid on the other side of the leision. Also, we started hydroxychloroquine sulfate 200mg/day with regular visits of ophthalmology for probable side effects of this drug.The lesions resolved with intralesional steroid injection during one month without pigmentation or other complications but on the other side, response to cryotherapy was slower and with undesirable dispigmentation (Figure 4). We continued monthly intralesional injections for some small resistant areas and after 4 months, the lesion was completely cleared. The patient was on hydroxychloroquine alone for an additional 4 months and at this time the patient was in good condition with no evidence of relapse.

DISCUSSION

Cutaneous Pseudolymphoma (PL) refers to a skin lesion that simulates clinical and histopatological features of true lymphoma. Cutaneous Lymphoid Hyperplasia (CLH) is the preferred term to describe the disease and its underlying pathogenesis because it refers to a benign reactive T-cell and B-cell collection [1].

The most common sites of involvement in pseudolymphoma (PL) are the face and the scalp [3]. Exposure to various stimuli can induce CLH. Known stimulants include arthropod bite, infection, drug, vaccinations, hyposensitization injection and

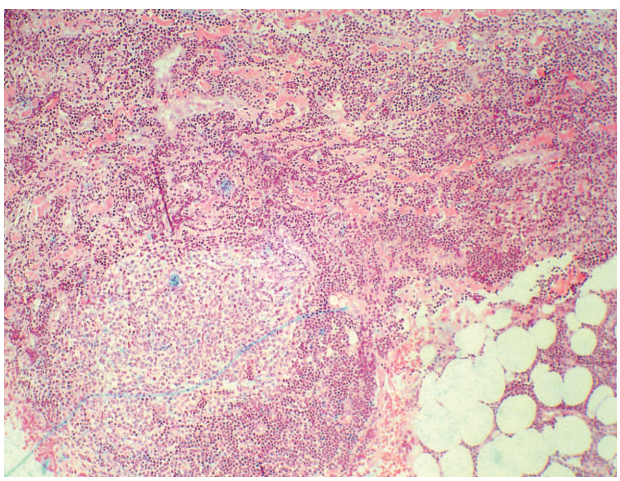

Figure 2. Dense lymphoid infiltrate in dermis with a prominent germinal center(H&E*10).

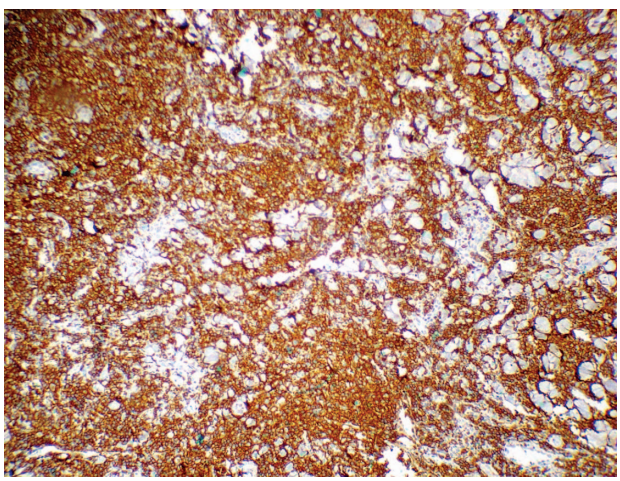

Figure 3. Dense B-Cell component is diffusely positive with CD-20 immunohistochemistry.

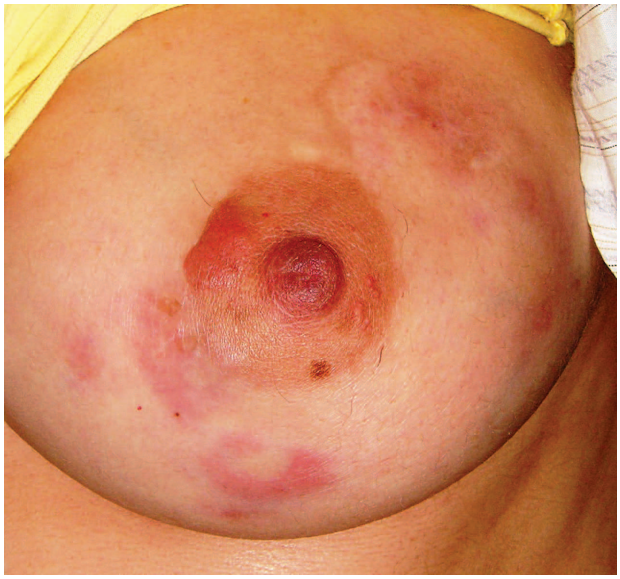

Figure 4. Good response of the lesion after intralesional steroid injections. Dispigmentation is seen due to cryotherapy.

tattoo [2]. In approaching a patient, it is important to recognize probable causative agents and rule out an underlying lymphoma by meticulous general examination. Drug induced PL is a rare form of cutaneous drug reaction which mimics a malignant lymphoma. At first, hypersensitivity reaction was believed to be the pathogenesis of drug induced PL but a recent study indicated that drugs may decrease immunological functions, leading to reactive proliferation of lymphocytes [4]. Our case had a long history of taking hormonal drugs but recovery did not occur after withdrawal, which is in opposition to the definition of drug induced CLH. Review of literature did not show any association between PL and hormonal drugs, with the exception of a report of cutaneous pseudolymphoma as an adverse reaction of tamoxifen in a 78- year-old woman [5]. It is not obvious whether or not these drugs can serve as a stimulating factor for PL and further in-depth researches are required to better elucidate this association.

In addition, general examination of the patient's organs revealed several masses with fibrocystic change in her breast. Although fibrocystic change should be excluded before the diagnosis of breast tissue pseudolymphoma is made [6], to our knowledge, our case is the first case of cutaneous pseudolymphoma of the breast in association with fibrocystic change.

Histologically, a dense lymphocytic infiltrate is seen within the dermis that can mimic T or B- cell lymphoma. It tends to be top heavy, although more diffuse infiltrations which extend to the subcutis can also be seen. In most cases, epidermis is intact and a narrow Grenz zone separates it from the below infiltrate [7], similar to the pathology of our case.

The prominent feature of pseudolymphoma is the polyclonal proliferation of T or B –cell. In T- cell PL, the infiltration may be band- like or nodular in distribution while in B- cell pseudolymphoma, the infiltration is typically nodular [8]. The differentiation of cutaneous B-cell lymphoid hyperplasia from malignant CBCLS is one of the most difficult problems in dermatology.

In our case, some histologic features were in favor of the diagnosis of cutaneous lymphoid hyperplasia including:

- Absence of nuclear atypia
- Presence of lymphoid follicles with germinal centers
- Lack of epidermotropism or adnexal invasion

Although these histological findings may be seen in low grade malignant B-cell lymphoma especially marginal zone B-cell lymphoma, other laboratory and molecular analyses including immunoglobulin gene rearrangement using PCR detected a polyclonal pattern which was more in favor of the benignity of the cellular infiltrate. It is important to emphasize that there are clear exceptions to each of the above mentioned criteria; therefore, the diagnosis of malignant or benign lymphoid hyperplasia depends on a constellation of clinical, histological, immunohistological and molecular features including follow-up information and response to treatment [9,10]. In CLH, if the offending agent is removed, the lesion usually resolves spontaneously within 6 to 8 weeks. In cases without an obvious cause, the clinical course tends to be chronic and indolent. Local treatment of persistent lesions includes intralesional corticosteroids, cryosurgery, local radiation or surgical excision [11]. Another valuable evidence of a benign condition in our case was lack of systemic disease, excellent treatment response and no recurrence during 8 months of follow-up.

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