Letter

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Primary cutaneous follicle center lymphoma of the breast: Management of an exceedingly rare malignancy

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SUMMARY Primary cutaneous follicle center lymphoma (PCFCL) is defined as a low-grade B-cell non-Hodgkin's lymphoma, which primarily occurs and remains confined to the skin, without evidence of extracutaneous or systemic involvement at the time of diagnosis. PCFCL affecting the breast skin is an exceedingly rare entity with only two cases reported in the English literature. We present a case of PCFCL affecting the periareolar breast skin and review the relevant literature. Our patient was a 64-year-old female who presented with an erythematous plaque in the periareolar region of the left breast. The diagnosis of PCFCL was confirmed by a biopsy performed with a seven-month delay, as the tumor had been initially misdiagnosed as a benign lesion. The patient was successfully treated with local radiation therapy. PCFCL is an indolent lymphoma associated with an excellent prognosis. For localized lesions, skin-directed therapies mainly consisting of radiation therapy or complete surgical excision are curative therapeutic approaches, while systemic chemotherapy should be reserved for patients with extensive disease. This case highlights the need to consider PCFCL as an important differential diagnosis in patients presenting with non-resolving erythematous breast skin lesions. A timely biopsy should be obtained to avoid delays in the initiation of appropriate treatment.

Keywords PCFCL, cutaneous, lymphoma, follicle, center, breast

Follicular lymphoma is the third most common lymphoma affecting the breast, accounting for 14-19% of all breast lymphomas and represents, in most cases, a manifestation of disseminated disease (*1*). Primary cutaneous follicle center lymphoma (PCFCL) involving the breast skin is an exceedingly rare clinical entity with only two cases reported in the English literature (*2,3*).

A 64-year-old woman presented with a 7-month history of a non-tender slowly enlarging erythematous plaque, in the areolar region of her left breast. She denied any symptoms, whereas her past medical history was unremarkable, and she had no family history of breast cancer. She had been prescribed local treatment by another institution without any clinical response.

Physical examination revealed a non-tender erythematous plaque, measuring approximately 4 cm, in the upper outer areolar region of the left breast (Figure 1). The mammogram was unremarkable, but the ultrasonogram showed a focal thickening of the outer aspect of the left areolar region. A biopsy was performed and the histological and immunohistochemical findings were suggestive of primary cutaneous follicle center lymphoma (Figure 2).

Following the biopsy, a thorough staging investigation was performed to rule out extracutaneous disease, including hematological and biochemical parameters, and computed tomography scans of the abdomen, chest, and pelvis. All of the above were unremarkable. The patient treated with superficial radiation therapy with a total dose of 3600 cGy delivered in 200 cGy doses for a total of 18 fractions. She exhibited a complete clinical response and is well without any evidence of tumor recurrence 27 months after treatment.

PCFCL is an indolent lymphoma of unknown histogenesis originating from the germinal-center B cells without evidence of extracutaneous disease at the

time of diagnosis. It most commonly occurs in patients in their fifth to seventh decades of life at a median age of 50 years, with a male to female ratio of 1.5:1 (*4,5*).

The most common clinical presentation of PCFCL is a solitary or less commonly multiple firm erythematous or violaceous papules, plaques, or tumors of variable size and a smooth surface (*6*). The lesions tend to enlarge slowly and may reach several centimeters in size. The most commonly affected areas are the head and neck, and the trunk (*3-5,7*). Multiple lesions are reported in 60% of the patients, 30-40% of which tend to occur in a localized area (*8*). Histologically, PCFCL is characterized by dense dermal infiltration of large centrocytes derived from germinal center B cells in a follicular, diffused, or mixed growth pattern (*8*). The neoplastic infiltrate spares the epidermis from which is separated by a grenz zone (*7,8*).

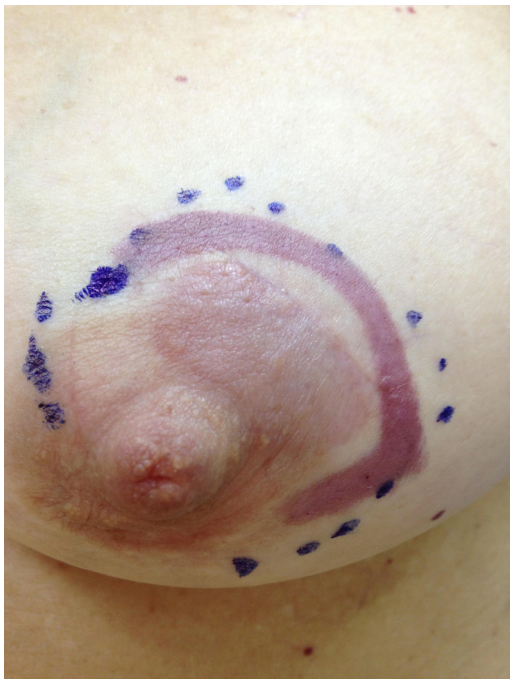

Figure 1. Photo showing the erythematous lesion of the left areolar region during radiation treatment planning.

On immunohistochemical analysis, the neoplastic lymphocytes express B-cell markers such as CD19, CD20, CD22, CD79A, and PAX5 and at least one follicle center marker which is BCL-6 and less commonly CD10 (*8,9*).

The differentiation of PCFCL from systemic follicular lymphoma (SCFL) is of paramount importance (*1*) since the two entities require different treatments (*7*).

The diagnosis of PCFCL is confirmed by an excisional on punch biopsy and subsequent thorough pathologic and immunohistochemical analysis. After the diagnosis of PCFCL is confirmed, a thorough staging investigation is mandatory to rule out extracutaneous involvement.

The treatment options for PCFCL depend on the extent of the disease and include local or systemic treatment. For solitary lesions, radiation therapy and complete surgical excision constitute curative therapeutic approaches (*6,8*). Surgical resection is considered for small well-demarcated solitary lesions (*6*).

Complete remission of PCFCL after radiation therapy is reported in up to 100% of the cases (*5*), whereas recent publications suggest that PCFCL can be successfully treated, with significantly lower doses of radiotherapy (*8*).

The prognosis of patients with PCFCL is excellent

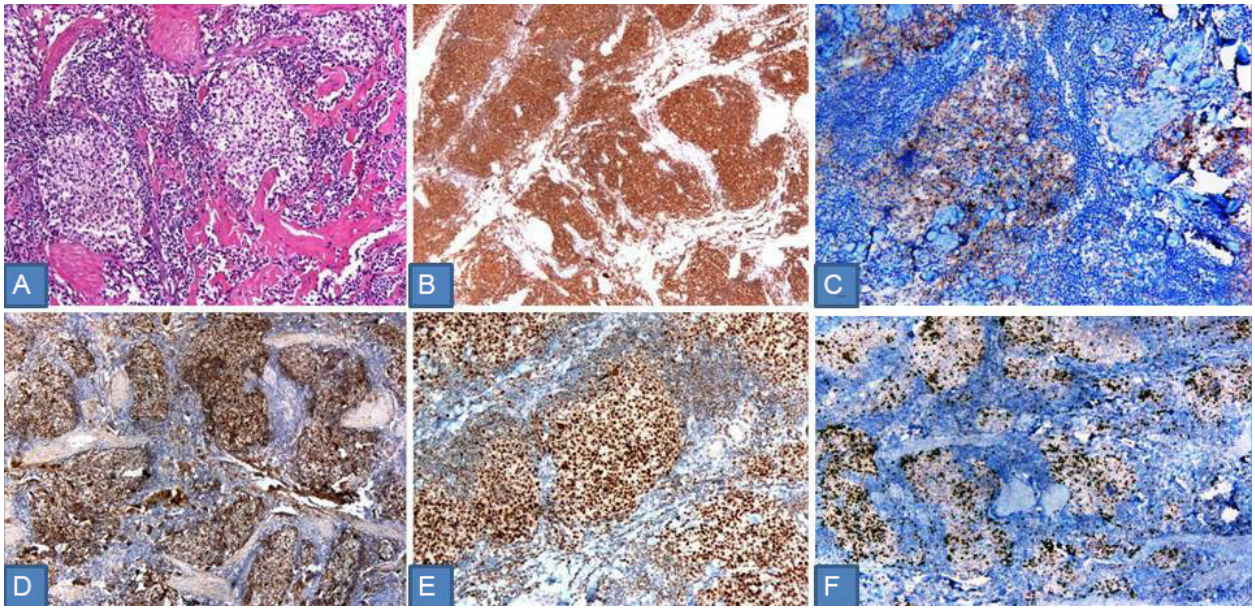

Figure 2. Histopathological and immunohistochemical findings of PCFCL. (A), Dermal lymphoid infiltrate with diffuse and nodular growth pattern (H&E ×20); **(B)**, Tumor cells showing strong and diffuse positive staining for CD20 (CD20 ×20); **(C)**, Negativity or focal weak positive staining for CD10 (CD10 ×40); **(D)**, Tumor cells stained positive for CD23 (CD ×20); **(E)**, Tumor cells stained positive for BCL-6 (BCL ×40); **(F)**, Reduced expression of ki-67 proliferation index in the nodules (Ki67 ×20).

even in cases with multifocal or recurrent disease, with a 5-year disease specific survival over 95% (*4,5,7,8*). Approximately 30% of the patients may exhibit a relapse (*5*). The extracutaneous spread most commonly involves the regional nodes and the bone marrow (*8*).

PCFCL may become locally aggressive if left untreated, whereas transformation to diffuse large B cell lymphoma has been suggested (*10*).

Although PCFCL involving the breast skin is exceedingly rare, a biopsy is indicated in any periareolar skin changes that do not resolve with topical treatment. Temporary resolution of the skin changes with or without topical treatment may occur, resulting in a delayed biopsy. A repeated biopsy should be considered in selected cases with discordance between clinical and pathological findings (*9*). In our patient, the biopsy was performed with a seven-month delay, as the tumor had been initially misdiagnosed as a benign lesion at another institution.

In conclusion, we present an exceedingly rare case of PCFCL affecting the periareolar breast skin. PCFCL is a clinical entity associated with an indolent clinical course and an excellent prognosis. A timely biopsy of any breast erythematous skin change that does not respond to local therapy should always be considered to avoid delays in initiating appropriate treatment.

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