

Regional Lymphomatoid Papulosis of the Breast Restricted to an Area of Prior Radiotherapy

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PRACTICE POINTS

- Cutaneous lesions of lymphomatoid papulosis (LyP) sometimes are confined to only one area of the skin, which is known as regional LyP.
- Patients with regional LyP have the same prognosis as those with widespread LyP, and no specific association has been reported with this clinical variant.
- Lesions of regional LyP respond to the same treatments as widespread LyP.

We report the case of a 59-year-old woman with type A regional lymphomatoid papulosis (LyP) that was localized to the left breast, a cutaneous area that had received radiotherapy for treatment of a carcinoma of the breast 5 years prior. This report is a rare example of regional LyP with all lesions located in an area of prior radiotherapy.

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Lymphomatoid papulosis (LyP) is a clinicopathologic variant of CD30⁺ primary cutaneous T-cell lymphoproliferative disorder characterized by a chronic, recurrent, self-healing eruption of papules and small nodules. From a clinical point of view, LyP is not considered a malignant disorder despite demonstration of clonality in most

cases.¹ From a histopathologic point of view, there are 5 types of LyP: (1) type A, the most common type, which is characterized by a wedge-shaped infiltrate composed of clustered large atypical cells admixed with neutrophils, eosinophils, histiocytes, and small lymphocytes; (2) type B, a rare variant characterized by a bandlike infiltrate of small- to medium-sized pleomorphic and hyperchromatic lymphocytes involving the superficial dermis with epidermotropism; (3) type C, which consists of a nodular infiltrate of large atypical cells with a cohesive arrangement closely similar to anaplastic large-cell lymphoma; (4) type D, a variant with histopathologic features that resemble primary cutaneous aggressive epidermotropic CD8⁺ cytotoxic T-cell lymphoma, but neoplastic cells express CD30 and a T-cell cytotoxic phenotype (β F1⁺, CD3⁺, CD4⁻, CD8⁺), and follow-up usually does not reveal development of systemic involvement or signs of other cutaneous lymphomas²; and (5) type E, which is characterized by oligolesional papules that rapidly ulcerate and evolve into large, necrotic, escharlike lesions with a diameter of 1 to 4 cm and an angiocentric and angiodestructive infiltrate of small- to medium-sized atypical lymphocytes expressing CD30 and frequently CD8.³

The clinical appearance of LyP usually is polymorphic, with lesions in different stages of evolution

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scattered all over the skin; however, the lesions are occasionally localized only to one area of the skin, the so-called regional or agminated LyP.⁴⁻¹⁴ We report a case of regional LyP that exclusively involved the skin of the left breast, which had previously received radiotherapy for treatment of breast carcinoma. Lymphomatoid papulosis with cutaneous lesions involving only an area of irradiated skin is rare.

Case Report

A 59-year-old woman presented with new-onset cutaneous lesions on the left breast. The patient had a history of invasive ductal carcinoma of the left breast, which had been treated 5 years prior with a partial mastectomy and radiotherapy (10 Gy per week for 5 consecutive weeks [50 Gy total]). Physical examination revealed a large nodular lesion with a necrotic surface on the upper half of the left breast as well as 3 small papular lesions with eroded surfaces on the lower half of the breast (Figure 1). A clinical diagnosis of cutaneous metastases from breast carcinoma was suspected.

Biopsies from one small papule and the large nodular lesion showed similar findings consisting of a necrotic epidermis covered by crusts and a wedge-shaped infiltrate involving the superficial dermis (Figure 2A). The infiltrate was mostly composed of large atypical mononuclear cells with oval to kidney-shaped nuclei, prominent nucleoli, and ample basophilic cytoplasm. Many mitotic figures were seen within the infiltrate (Figure 2B). The infiltrate of atypical cells was admixed with small lymphocytes, histiocytes, and some eosinophils. Immunohistochemically, the large atypical cells expressed CD2, CD3, CD4, CD45, CD30, and epithelial membrane antigen (Figures 2C and 2D). A few atypical cells also expressed CD8 and T-cell intracellular antigen 1. Approximately 60% of the nuclei of the atypical cells showed MIB-1 positivity, while CD20, CD56, AE1/AE3, S-100 protein, CD34, and CD31 were negative. The anaplastic lymphoma kinase was not expressed in atypical cells. Monoclonal rearrangement of the γ T-cell receptor was demonstrated on polymerase chain reaction. Physical examination showed no lymphadenopathy in any lymph node chains. Computed tomography of the chest and abdomen failed to demonstrate systemic involvement. On the basis of these clinical, histologic, immunohistochemical, and molecular results, a diagnosis of type A regional LyP was established.

The patient was treated with 2 daily applications of clobetasol propionate cream 0.5 mg/g and 10 mg of oral methotrexate per week for 4 weeks. After 4 weeks of treatment, the lesions on the left



Figure 1. Three small papular lesions on the left breast (A). Close-up view of a large nodular lesion with a necrotic surface on the upper half of the breast (B).

breast had resolved leaving slightly atrophic scars. Six months later, an episode of recurrent papular lesions occurred in the same area and responded to the same treatment, but no systemic involvement had been found.

Comment

Regional LyP is a rare variant, with only a few reported cases in the literature.⁴⁻¹⁸ Scarisbrick et al⁴ originally reported 4 patients with LyP limited to specific regions. Interestingly, one of the patients had mycosis fungoides and the LyP lesions were confined to the same region where the mycosis fungoides lesions were observed.⁴ In a review of LyP in patients from the Netherlands (n=118), lesions limited to a specific region of the body were observed in 13% of cases.⁵ Cases of LyP limited to

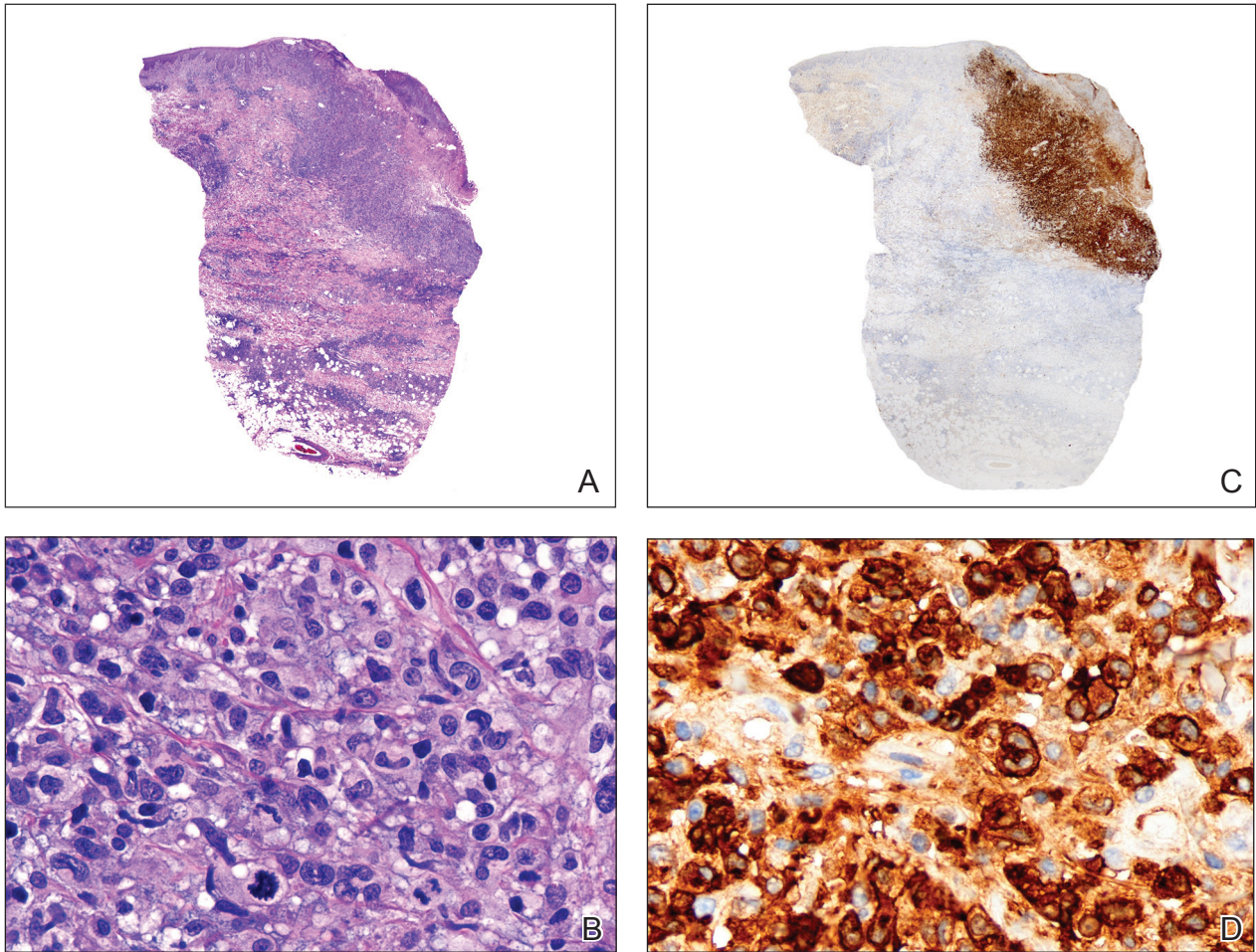


Figure 2. Biopsy demonstrated an ulcerated epidermis and a wedge-shaped infiltrate involving the superficial dermis (A)(H&E, original magnification $\times 10$). Higher magnification demonstrated atypical mononuclear cells with frequent mitotic figures (B)(H&E, original magnification $\times 400$). Immunohistochemical staining of the same biopsy was positive for CD30 (C)(original magnification $\times 10$). Almost all cells of the infiltrate expressed CD30 immunoreactivity (D)(original magnification $\times 400$).

acral skin also have been reported.⁶⁻⁸ Heald et al⁹ described 7 patients who had continuing eruptions of papulonodules with histopathologic features of LyP within well-circumscribed areas of the skin. The investigators interpreted this localized variant of LyP as an equivalent of the limited plaque stage of mycosis fungoides. Interestingly, one of the patients with LyP eventually developed plaques of mycosis fungoides in other areas of the skin not involved by LyP.⁹ Sharma et al¹⁰ described an additional example of regional LyP, and Nakahigashi et al¹¹ described a patient with tumor-stage mycosis fungoides who subsequently developed regional LyP involving the right side of the chest. Kim et al¹² described a patient with recurrent episodes of regional LyP exclusively involving the periorbital skin, and Torrelo et al¹³ reported a 12-year-old boy with persistent lesions

of LyP involving the skin of the right side of the abdomen. Coelho et al¹⁴ reported a 13-year-old adolescent girl who presented with recurrent papules of LyP exclusively involving the left upper arm. Buder et al¹⁵ reported a case of LyP limited to Becker melanosis. Shang et al¹⁶ described an additional case of regional LyP that was successfully controlled by interferon alfa-2b and nitrogen mustard solution. Haus et al¹⁷ reported type A LyP confined to the cutaneous area within a red tattoo. Finally, Wang et al¹⁸ reported a case of regional LyP in association with pseudoepitheliomatous hyperplasia.

Several dermatoses may appear as specific isomorphic responses to various external stimuli, and it is possible that radiotherapy induces some damage that favors the location of the lesions because the irradiated skin behaves as a locus minoris resistentiae.

Pemphigus vulgaris,^{19,20} Sweet syndrome,²¹ cutaneous angiosarcoma,²²⁻³² and cutaneous metastases from malignant melanoma also have been reported to be confined to irradiated skin.³³ However, in our PubMed search of articles indexed for MEDLINE using the terms *lymphomatoid papules* and *regional*, none of the previously reported cases of regional LyP had a history of radiotherapy, and in no instance did the lesions develop on a previously irradiated area of the skin.⁴⁻¹⁸ The localization of the lesions in our patient could have been the result of the so-called radiation recall phenomenon. Recall dermatitis is defined as a skin reaction in a previously irradiated field, usually subsequent to the administration of cytotoxic drugs or antibiotics.³⁴ It may appear days to years after exposure to ionizing radiation and has mostly been associated with chemotherapy drugs, but recall dermatitis is neither exclusive of chemotherapy medications nor strictly radiotherapy induced. The concept of recall dermatitis has been expanded beyond radiation recall dermatitis to include dermatitis induced by other stimuli, including other drugs, contact irritants, and UV radiation, as well as residual herpes zoster. Nevertheless, in recall dermatitis the triggering drug or agent recalls a prior dermatitis in the involved area, such as sunburn or radiodermatitis. In our patient, there was no history of LyP prior to irradiation of the left breast; therefore, the most plausible interpretation of the peculiar localization of the lesions in our patient seems to be that the eruption resulted as expression of a locus minoris resistentiae.

Distinction between primary cutaneous anaplastic large-cell lymphoma and LyP may be difficult because the histopathologic and immunophenotypic features may overlap. In our case, the presence of several papular lesions and one large nodule are more consistent, from a clinical point of view, with a diagnosis of LyP rather than primary cutaneous anaplastic large-cell lymphoma, which usually presents with a solitary and often large, ulcerated, reddish brown tumor. In our patient, the absence of lymphadenopathy, negative results of the computed tomography of the chest and abdomen, and lack of expression for anaplastic lymphoma kinase in atypical cells of the infiltrate militate against a diagnosis of secondary cutaneous involvement from nodal disease.

The histopathologic differential diagnosis of the current case also included cutaneous CD30⁺ epithelioid angiosarcoma of the breast. Weed and Folpe³⁵ reported the case of an 85-year-old woman who developed a CD30⁺ epithelioid angiosarcoma on the breast after undergoing breast-conserving surgery and adjuvant radiotherapy for treatment of an infiltrating ductal carcinoma of the breast.

Histopathology showed a diffuse replacement of the dermis by a highly malignant-appearing epithelioid neoplasm growing in a solid sheet. Neoplastic cells expressed strong CD30 immunoreactivity with absence of immunoreactivity for cytokeratins, S-100 protein, and CD45. Additional immunostaining demonstrated that neoplastic cells also expressed strong immunoreactivity for CD31 and the friend leukemia virus integration 1 gene, *FLI-1*, and focal positivity for von Willebrand factor, supporting a diagnosis of epithelioid angiosarcoma.³⁵ In our patient, CD34 and CD31 were negative, which ruled out the endothelial nature of neoplastic cells.

Conclusion

In summary, we report an example of regional LyP limited to the left breast of a woman with a history of partial mastectomy and adjuvant radiotherapy for treatment of invasive ductal breast carcinoma. It is a rare case of regional LyP exclusively involving an irradiated area of the skin.

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