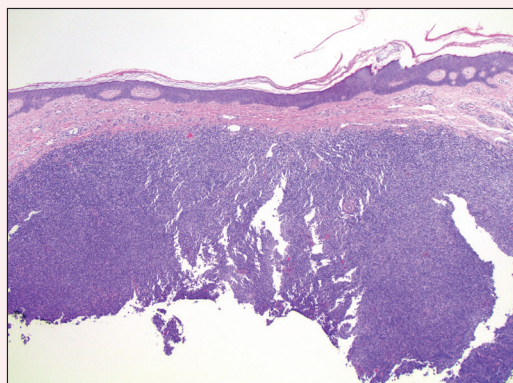


# Erythematous Pearly Papule on the Chest

Nikoleta Brankov, MD; Amandeep Sandhu, MD; Justin Kerstetter, MD; Nancy Anderson, MD

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H&E, original magnification  $\times 4$ .

An 81-year-old man with a history of hyperthyroidism, paroxysmal atrial fibrillation, hypertension, and nonmelanoma skin cancer presented with an erythematous pearly papule on the right lateral chest of 1 year's duration. The patient reported no symptoms of pruritus, bleeding, or burning. He was otherwise asymptomatic, and a review of systems revealed no abnormalities. His current medications included aspirin, benazepril, finasteride, levothyroxine, tamsulosin, warfarin, and alprazolam. He denied any new medications, recent travel, or preceding trauma. He had

a history of Agent Orange exposure. Physical examination revealed a 0.4-cm erythematous pearly papule on the right lateral chest. A shave biopsy was obtained.

## The best diagnosis is:

- granuloma faciale
- leukemia cutis
- lymphomatoid papulosis
- Merkel cell carcinoma
- primary cutaneous B-cell lymphoma

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The authors report no conflict of interest.

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## Primary Cutaneous B-cell Lymphoma

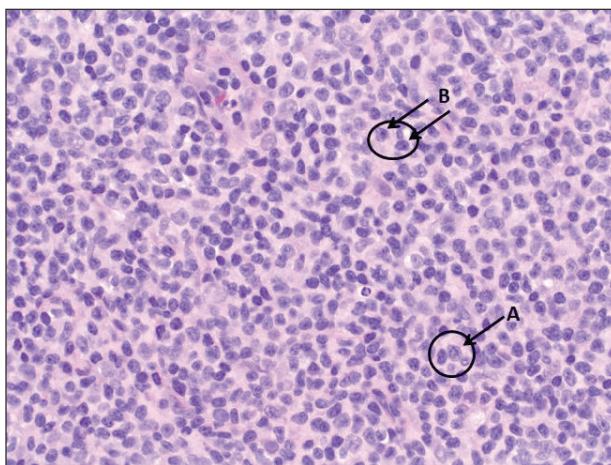
Cutaneous B-cell lymphomas (CBCLs) are a diverse but rare group of cutaneous lymphoproliferative neoplasms that make up approximately 20% of the total number of hematolymphoid neoplasms primary to the skin.<sup>1</sup> These lymphomas are comprised of neoplastic B cells in various stages of differentiation. As a whole, they are rare neoplasms that primarily involve the head, neck, trunk, arms, or legs.<sup>1</sup> Clinically, patients present with nontender, compressible, solitary, red to violaceous papules or nodules. Most CBCLs are considered low-grade malignancies with nonaggressive behavior and excellent prognosis; however, the diffuse large B-cell lymphomas, including but not limited to intravascular and leg type; lymphomatoid granulomatosis; and B-cell lymphoblastic lymphoma can act more aggressively.<sup>1</sup>

Histopathologic examination of primary CBCL generally reveals a relatively normal epidermis accompanied by a nodular to diffuse monomorphic lymphocytic cellular infiltrate in the dermis that can occasionally extend into the subcutaneous tissue (quiz image). Although not specific for CBCLs, oftentimes there is an acellular portion of the superficial papillary dermis known as a grenz zone that can serve as a histopathologic clue to the diagnosis of a cutaneous lymphoproliferative disorder. The list of malignant B-cell neoplasms is extensive (eg, cutaneous marginal zone B-cell lymphoma, primary cutaneous follicle center lymphoma, diffuse large B-cell lymphoma, intravascular large B-cell lymphoma), and few are seen in the skin.

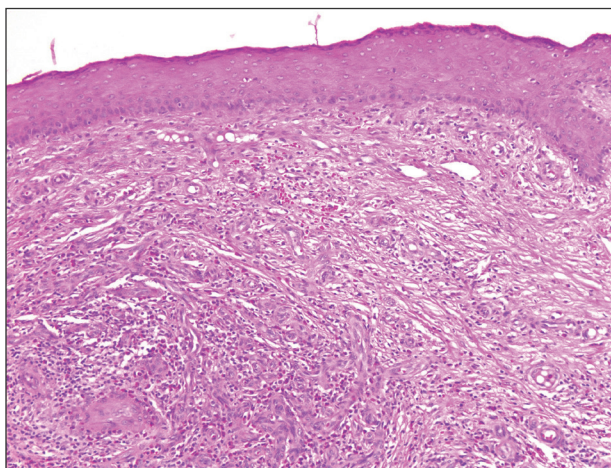
The most common type of CBCL is marginal zone B-cell lymphoma, which is considered to be a tumor of mucosa-associated (or skin-associated) lymphoid tissue. It is characterized by a monomorphic population of small mature lymphocytes showing characteristics of the B cells of the marginal zone of the lymph node. Some cells have the features of centrocytes/centroblasts (Figure 1) demonstrated by slightly irregular or indented nuclei and generous amounts of cytoplasm. Larger and more pleomorphic cells such as immunoblasts are similarly noted (Figure 1). The quiz image and Figure 1 demonstrate a cutaneous marginal zone B-cell lymphoma. A histomorphologic clue supporting a diagnosis of marginal zone B-cell lymphoma over reactive lymphoid hyperplasia is a B-cell predominate (B- to T-cell ratio of at least 3 to 1) infiltrate that is comprised of marginal zone-type cells. Immunohistochemistry demonstrating fewer

differentiated B cells with light chain restriction may provide additional evidence that supports a clonal and potentially malignant process.

Erythematous to violaceous nodules on the head and neck of older individuals are characteristic of both granuloma faciale and CBCL. Histologically, granuloma faciale is characterized by a dense cellular infiltrate, often with a nodular outline, occupying the mid dermis.<sup>2</sup> Granuloma faciale typically spares the immediate subepidermis and hair follicles,



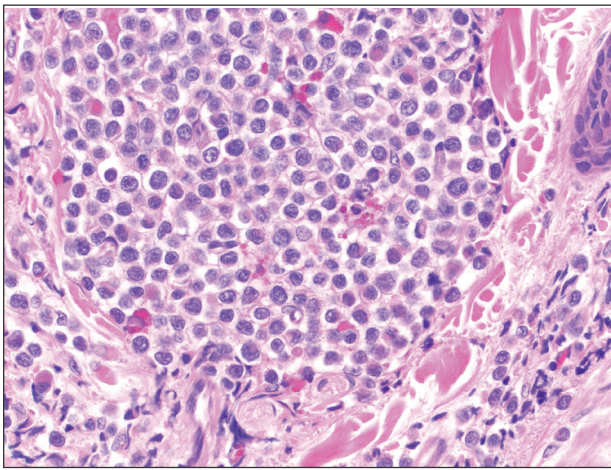
**Figure 1.** Monomorphous populations of lymphoid cells characteristic of marginal zone B-cell lymphoma: centroblastlike cells (arrow A) and immunoblastlike cells (arrow B)(H&E, original magnification  $\times 20$ ).



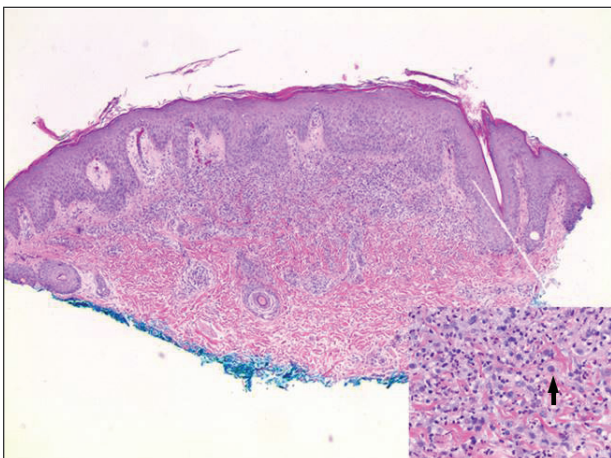
**Figure 2.** Granuloma faciale shows a normal epidermis with a grenz zone present above a diffuse mixed infiltrate of dermal neutrophils, eosinophils, lymphocytes, and histiocytes in a vasculocentric pattern with early concentric fibrosis (H&E, original magnification  $\times 4$ ).

forming a grenz zone. The cellular infiltrate is polymorphic and consists of eosinophils and neutrophils with scattered plasma cells, mast cells, and lymphocytes in a vasculocentric distribution, eventually with chronic concentric fibrosis (Figure 2).

Leukemia cutis demonstrates a dermal infiltrate that contains atypical mononuclear cells (myeloblasts and myelocytes)(Figure 3).<sup>3</sup> These markedly atypical mononuclear cells can have kidney bean-shaped nuclei and percolate through the dermal collagen, resembling single-file cells. They have increased nuclear to cytoplasmic ratios and occasionally have prominent nucleoli. Correlation



**Figure 3.** Leukemia cutis (acute myelomonocytic leukemia) shows a solid cluster of immature blasts with a monocytyoid appearance with adjacent single filing (H&E, original magnification  $\times 40$ ).



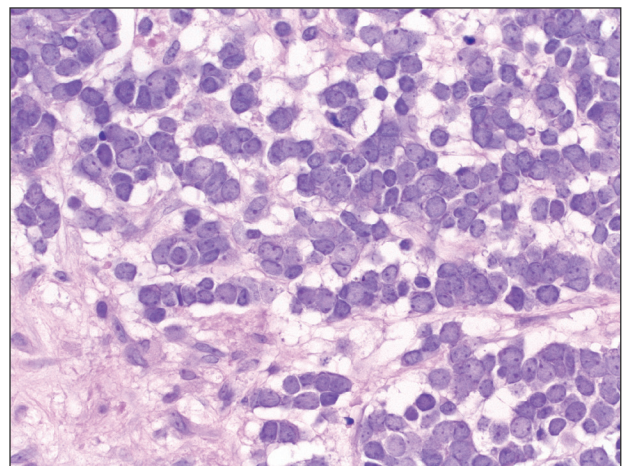
**Figure 4.** Lymphomatoid papulosis (from the family of cutaneous CD30<sup>+</sup> lymphoproliferative disorders) shows epidermal hyperplasia with interstitial and a diffuse dermal infiltrate of large atypical lymphoid cells (inset arrow [H&E, original magnification  $\times 40$ ]). The large cells stain positively for CD30 (H&E, original magnification  $\times 4$ ).

with immunophenotypic and cytochemical studies is required for specific typing of the leukemic infiltrate.

Similar to primary CBCL, lymphomatoid papulosis (LyP) consists of erythematous papules or nodules that can occur anywhere on the body. In contrast to CBCL, the lesions of LyP classically self-resolve. However, approximately 10% to 20% of patients develop a malignant lymphoma, with mycosis fungoides, Hodgkin disease, and anaplastic large cell lymphoma being the most commonly associated.

Histologic examination of lesions of LyP classically demonstrates a wedge-shaped dermal infiltrate with variable epidermal changes (Figure 4). The wedge-shaped infiltrate is composed of large atypical cells. Three main types of lesions have been delineated: types A, B, and C. Type A is characterized by an increased number of cells with large vesicular nuclei with clumped chromatin, prominent nucleoli, and pronounced cytoplasm. Reed-Sternberg–like cells with an admixture of inflammatory cells including small lymphocytes, macrophages, neutrophils, and eosinophils also are present. Type B neoplastic cells vary in size and feature hyperchromatic, convoluted, or cerebriform nuclei. The infiltrate can be dense and bandlike with fewer cells resembling mycosis fungoides; type B LyP has neoplastic cells, not inflammatory cells. Finally, type C demonstrates solid sheets of large atypical cells resembling anaplastic large cell lymphoma. Immunohistochemically, the atypical cells often are CD4<sup>+</sup> and CD8<sup>-</sup> with variable loss of pan-T-cell antigens. The atypical cells of types A and C express CD30 reactivity.<sup>4</sup>

Merkel cell carcinoma (MCC) is a primary neuroendocrine carcinoma of the skin that usually arises



**Figure 5.** Merkel cell carcinoma shows finely dispersed salt-and-pepper chromatin and molded nuclear contour. The tumor cells are positive for synaptophysin and show dotlike positivity for cytokeratin 20 (H&E, original magnification  $\times 40$ ).

on sun-exposed skin in elderly patients with lesions that histologically and clinically resemble cutaneous lymphoma.<sup>5</sup> It classically is composed of small, round to oval, basophilic cells with a vesicular nucleus and multiple small nucleoli. Apoptotic cells and mitoses often are present.<sup>6</sup> One key finding that helps to differentiate MCC from lymphoma is the presence of finely dispersed salt-and-pepper chromatin and molded nuclear contour in MCC (Figure 5).

Immunophenotyping is important in the differentiation of these diagnoses. The atypical cells of LyP are positive for CD3, CD4, and CD30 but are negative for CD8. However, in type B LyP, the large CD30<sup>+</sup> cells seen in the other types are not commonly seen. In contrast, MCC expresses reactivity with cytokeratins, in particular cytokeratin 20 and CAM5.2, classically in a paranuclear dotlike pattern. In keeping with MCC's neuroendocrine differentiation, the tumor cells will demonstrate reactivity with synaptophysin, chromogranin, and CD56. The immunohistochemistry for leukemia cutis varies depending on the type of leukemia. Acute myelomonocytic leukemia is positive for myeloperoxidase, CD13, CD33, and CD68. The immunophenotype

of these marginal zone lymphoma cells is as follows: positive for CD20, CD79a, and Bcl-2; negative for Bcl-6, CD5, CD10, CD23, and cyclin D1 (Bcl-1).<sup>7</sup>

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