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Primary cutaneous marginal-zone lymphoma

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Abstract

Primary cutaneous B cell lymphomas (PCBCL) are the second most common type of primary cutaneous lymphoma. The three main types of PCBCL are primary cutaneous marginal-zone lymphoma (PCMZL), primary cutaneous follicle-center lymphoma, and primary cutaneous diffuse large B-cell lymphoma, leg type. PCMZL has an indolent course with a five-year survival rate approaching 99%. Lesions most often present on the trunk or arm as erythematous-to-violaceous papules, plaques, or nodules. Approximately one-half of patients have solitary skin lesions. Treatment options include surgery, radiation, and topical, intralesional or systemic therapy. We present the case of a 33-year-old Hispanic woman with firm, pruritic, pink papules on the forehead and cheeks, who was diagnosed with PCMZL.

Case Presentation

PATIENT: 33-year-old woman
DURATION: Five years
DISTRIBUTION: Forehead, glabella, nose, and cheeks

HISTORY: A 33-year-old Hispanic woman was referred to the Dermatology Clinic at Bellevue Hospital Center for a two-year history of pruritic, erythematous papules on the forehead and cheeks. A punch biopsy was performed that was consistent with pseudolymphoma.

The patient was initially treated with doxycycline for three months, but had no response. She subsequently was treated with five cycles of intralesional triamcinolone, resulting in resolution of the papules. Four months later, she presented with new pruritic papules in the same distribution. She was again treated with several cycles of intralesional triamcinolone, and also started on hydroxychloroquine. The patient reported less pruritus, but continued to develop new papules. A repeat biopsy from the nasal bridge was performed

PHYSICAL EXAMINATION: On the forehead, glabella, nose, and cheek were firm, pink, 1 mm to 3 mm papules with no epidermal changes (**Figures 1 and 2**). No other suspicious lesions were present on total skin examination. The patient had no cervical, axillary, or inguinal lymphadenopathy, or hepatosplenomegaly.

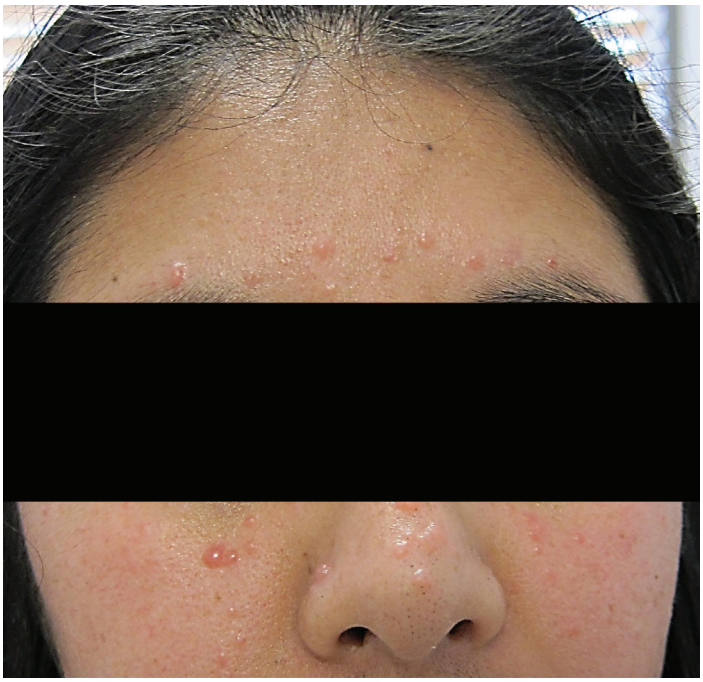

Figure 1. Firm, pink, 1 mm to 3 mm papules on the forehead, glabella, nose and cheek.

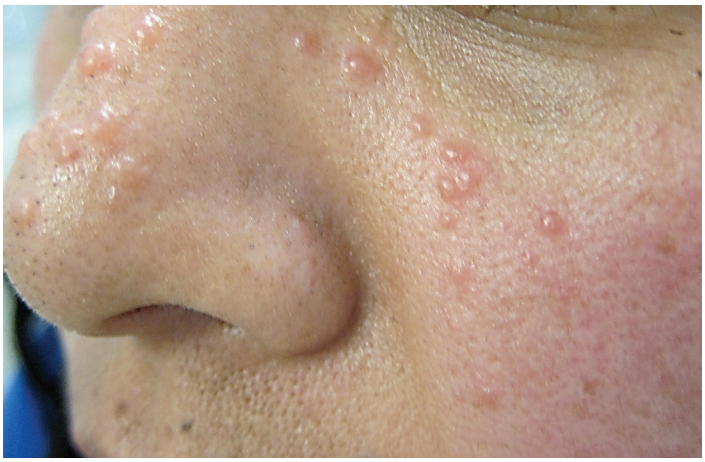

Figure 2. Firm, pink, 1 mm to 3 mm papules with no epidermal changes on the nose and cheek.

LABORATORY DATA: A complete blood count, a blood chemistry panel, and liver function tests were normal.

HISTOPATHOLOGY: There is a nodular infiltrate of predominantly CD20(+) small B cells (**Figure 3**) with abberant expression of bcl-2. CD138 highlights the plasma cells, and there is a slight predominance of lambda light-chain staining cells over kappa light-chain staining cells.

DIAGNOSIS: Primary cutaneous marginal-zone lymphoma

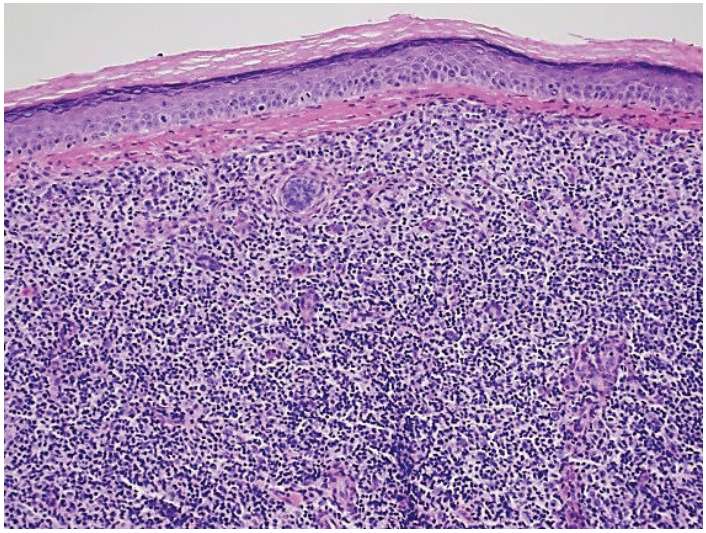

Figure 3. Biopsy showing a nodular infiltrate of predominantly CD20(+) small B cells.

Discussion

Primary cutaneous B cell lymphoma (PCBCL) is the second most common type of primary cutaneous lymphoma and accounts for approximately 25-29% of cases [1, 2]. In 2005, the World Health Organization and European Organization for the Research and Treatment of Cancer (EORTC) devised a classification system that distinguishes the three main types of PCBCL: primary cutaneous marginal-zone lymphoma (PCMZL), primary cutaneous follicle-center lymphoma (PCFCL), and primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT) [1]. PCMZL and PCFCL follow an indolent course, while PCDLBCL-LT is aggressive and carries a poor prognosis.

PCMZL presents on the trunk (46%), arm (17%), or head (13%) as erythematous to violaceous papules, plaques, or nodules [3]. Approximately one-half of patients present with a solitary lesion. Men develop PCMZL twice as often as do women. The median age at diagnosis is 55 years [4]. In pediatric patients, PCMZL has a natural history similar to adult patients with PCMZL [5]. Older patients with PCMZL on the head or neck have an increased risk of concomitant nodal disease [6]. The five-year survival rate for PCMZL is 99% [1, 7, 8]. Spontaneous remission occasionally occurs, particularly during the first months of the disease [1].

The diagnosis of PCMZL is made by skin biopsy. A biopsy containing reticular dermis and fat helps to distinguish PCMZL from a reactive or inflammatory process. The histopathologic features of PCMZL show a patchy, nodular, or diffuse infiltrate involving the dermis and subcutaneous fat, with sparing of the epidermis. The infiltrate is surrounded by marginal B cells, which are pale-staining small- to medium-sized cells with indented nuclei, inconspicuous nucleoli, and abundant pale cytoplasm. These cells stain positive for CD20, CD79a, and Bcl-2, and negative for CD5, CD10, and Bcl-6 [9].

All patients with PCMZL should undergo a comprehensive work-up to distinguish primary cutaneous disease from systemic marginal zone lymphoma with secondary cutaneous involvement. A complete history and physical examination

should be performed, including palpation for lymphadenopathy and hepatosplenomegaly. The recommended laboratory work-up includes a complete blood count with differential analysis, a comprehensive metabolic profile, and a lactate dehydrogenase level. An association between PCMZL and *Borrelia burgdorferi* infection has been reported in Europe, but not in the United States [10-13]. While some authors recommend obtaining Lyme titers in all patients with PCMZL, others advocate only obtaining them in those from endemic areas [4, 11].

Integrated contrast enhanced computed tomography/positron emission tomography (PET-CT) is the standard modality for investigating extracutaneous involvement, and should be performed in all patients. A biopsy should be performed on any lymph node that is larger than 1.5 cm or with high metabolic activity on a PET scan [4]. Peripheral flow cytometry or a bone-marrow biopsy should be considered if there is heightened concern for systemic involvement [14].

Treatment of PCMZL is based on small, retrospective studies and institutional experience, as there have been no randomized, controlled trials due to the rarity of the disease. Surgery and radiotherapy are ideal treatment options for patients with isolated lesions, as these modalities are often curative. In 39 patients with PCMZL, surgical excision provided a 97.4% complete response rate with a 31.6% recurrence rate. Radiation therapy provided a 97.6% complete response rate in 83 patients with PCMZL, with a 46.9% recurrence rate [3]. Topical agents are ideal for patients with multifocal disease. Class I topical glucocorticoids can induce complete responses in some patients [15, 16]. Other treatment options include topical nitrogen mustard, topical imiquimod, intralesional triamcinolone, intralesional interferon, and cryotherapy [8, 17-19]. In two separate studies, rituximab induced a complete response in four of five patients when administered intralesionally and in one of five patients when administered systemically [20, 21]. Due to the indolent nature of PCMZL and the possibility of spontaneous resolution, observation is an alternative option for carefully selected patients. While the EORTC recommends the use of antibiotics in patients with PCMZL and *Borrelia* antibodies, this is generally not advocated in the United States and is not mentioned in the National Comprehensive Cancer Network Guidelines [8, 17].

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