

# A case report of primary cutaneous marginal zone B-cell lymphoma with mastocytosis

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## Abstract

A 53-year-old man presented with asymptomatic, dusky reddish nodules on his trunk, which had persisted for 7 years. Histological findings showed nodular to diffuse dermal infiltration of lymphocytes with irregular nuclei, eosinophils, plasma cells, and mast cells. CD20 revealed patch positivity. Periphery of lymphoid follicles showed BCL-2 positivity and BCL-6 positivity focally at the center. CD30 and toluidine blue staining showed positivity, and several mast cells were confirmed. The immunoglobulin heavy chain gene rearrangement result showed B-cell monoclonality. The patient's condition was diagnosed as cutaneous marginal zone B-cell lymphoma, plasmacytoid type with mastocytosis. Primary cutaneous marginal zone B-cell lymphoma is an indolent lymphoma with a tendency for local recurrence. In the specimen obtained from our patient, multiple mast cells were observed. Primary cutaneous marginal zone B-cell lymphoma with prominent mastocytosis is rare and there are a few reported cases. Therefore, this case is worth reporting for its rarity and for the purpose of reminding mastocytosis in primary cutaneous marginal zone B-cell lymphoma.

## Keywords

B-cell lymphoma, mastocytosis, plasma cells

## Introduction

Primary cutaneous lymphomas (PCLs) are the most frequent extra-nodal lymphomas. Primary cutaneous B-cell lymphoma (PCBCL) is a heterogeneous group of mature B-cell neoplasms with tropism for the skin, with a rate of only 5%–10% in the East.<sup>1</sup> Compared with T-cell lymphoma (TCL), PCBCL has a short history of 1–2 years and a rapidly growing single tumor form. Primary cutaneous marginal zone B-cell lymphoma (PCMZL) is included as one of the most common types of PCBCL in the revised World Health Organization–European Organization for Research and Treatment of Cancer classification for cutaneous lymphomas.<sup>2</sup>

## Case report

A 53-year-old man presented with asymptomatic, multiple, dusky reddish nodules on his trunk, which had persisted for 7 years (Figure 1(a) and (b)). The lesions were bilaterally distributed over the lateral side of the trunk, and they had spread slightly. The patient reported a history of arterial hypertension and type 2 diabetes mellitus and had no systemic symptoms suggestive of other organ involvement. He

reported no induction or exacerbation of symptoms by specific triggers. After stroking lesions, the skin becomes swollen, itchy, and red. Histological findings of the biopsy specimen showed nodular to diffuse dermal infiltration of lymphocytes with irregular nuclei, eosinophils, plasma cells, and mast cells (Figure 2(a)–(c)). Considering the clinical manifestations and histological features of extensive mast cell infiltration, the lesion corresponded to urticaria pigmentosa (UP). However, from histological findings, monocytic lymphocytes with more abundant cytoplasm and uniform population than other cells were observed in some areas. Kappa light chain restriction was suggested in the immunostaining results of the immunoglobulin (Ig) light chain (Figure 2(h) and (i)). CD20 staining, a B-cell marker, revealed reactive lymphoid follicles

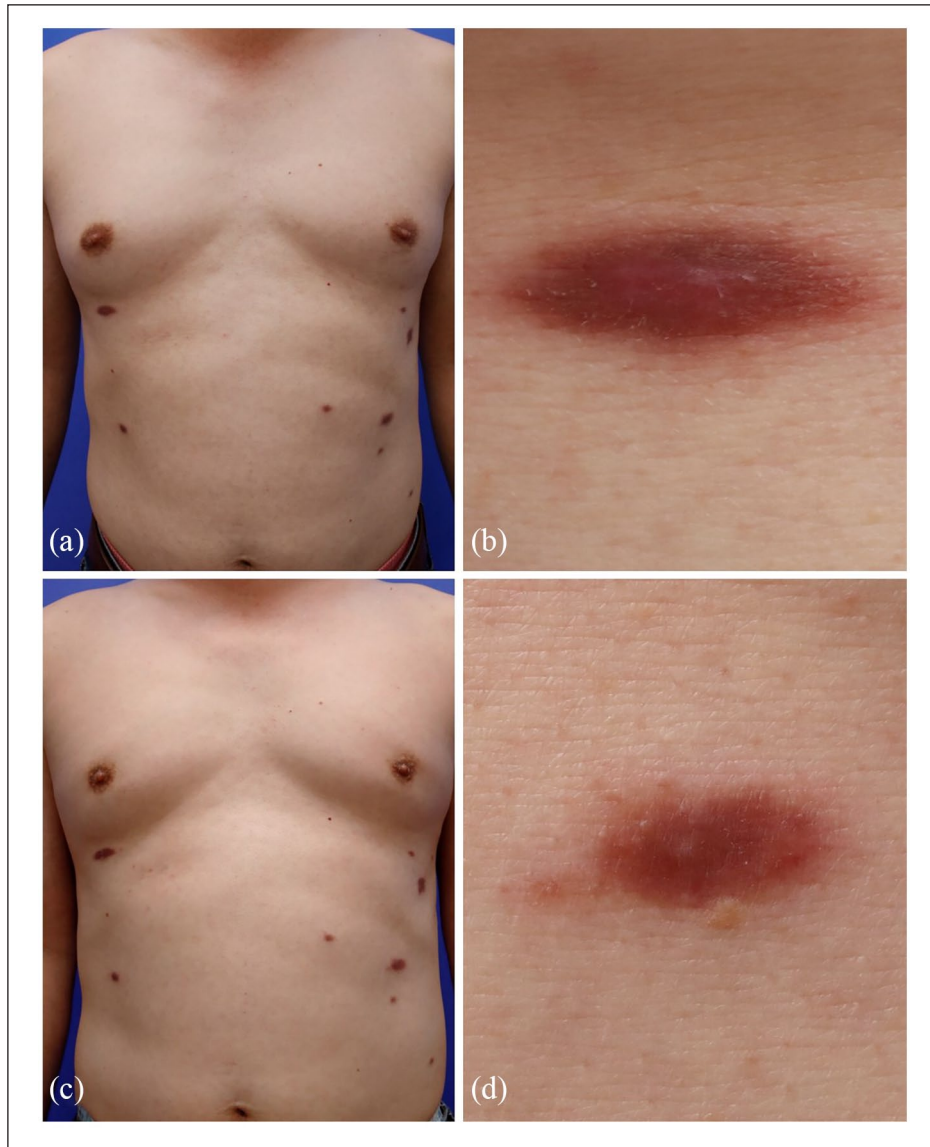
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**Figure 1.** (a) Multiple, dusky reddish, irregular shaped nodules with fine scales bilaterally distributed over the trunk. (b) Close-up view shows an oval-shaped nodule with fine scales. (c, d) After 9 months of treatment, the lesions became smaller and flatter.

with patch positivity (Figure 3(b)). Periphery of lymphoid follicles showed BCL-2 positivity (Figure 3(d)) and BCL-6 positivity focally at the center (Figure 3(c)). Toluidine blue (Figure 2(d)) and CD117 (Figure 2(e)) staining showed positivity, and several mast cells were confirmed. MUM1 and CD138 (Figure 2(f) and (g)) showed diffuse positivity and confirmed positive reaction in plasma cells. The Ig heavy chain gene rearrangement result showed B-cell monoclonality. Of the Igs measured in serum, only the IgG level was elevated to 1905.80 mg/dL. Peripheral blood smear and immunofixation electrophoresis results in serum and urine showed no abnormality. The patient did not show any evidence of hypermetabolic metastasis on whole body positron emission tomography (PET)/computed tomography

(CT). Finally, the patient was diagnosed as having PCMZL, plasmacytoid type with mastocytosis by dermatology and hemato-oncology examinations.

## Discussion

Mastocytosis is a rare heterogeneous disorder characterized by excessive proliferation and accumulation of pathological mast cells in the skin, bone marrow, gastrointestinal (GI) tract, liver, spleen, and lymphatic tissues.<sup>3,4</sup> The skin is the most common site of involvement. Among the classification of cutaneous mastocytosis, multiple lesions range from less than 10 to greater than 100 which is referred to as UP.<sup>5</sup> Clinical features of UP include small, monomorphic tan to brown

macules or papules distributed mostly on the trunk. The palms, soles, face, and scalp are generally spared. Systemic symptoms can occur such as pruritus, flushing, abdominal pain, diarrhea, palpitations, dizziness, and syncope. Fever, night

sweats, bone pain, epigastric distress, malaise, and weight loss often indicate the presence of extracutaneous disease.<sup>4</sup>

PCMZL is an indolent lymphoma with a tendency for local recurrence, but extracutaneous dissemination is very

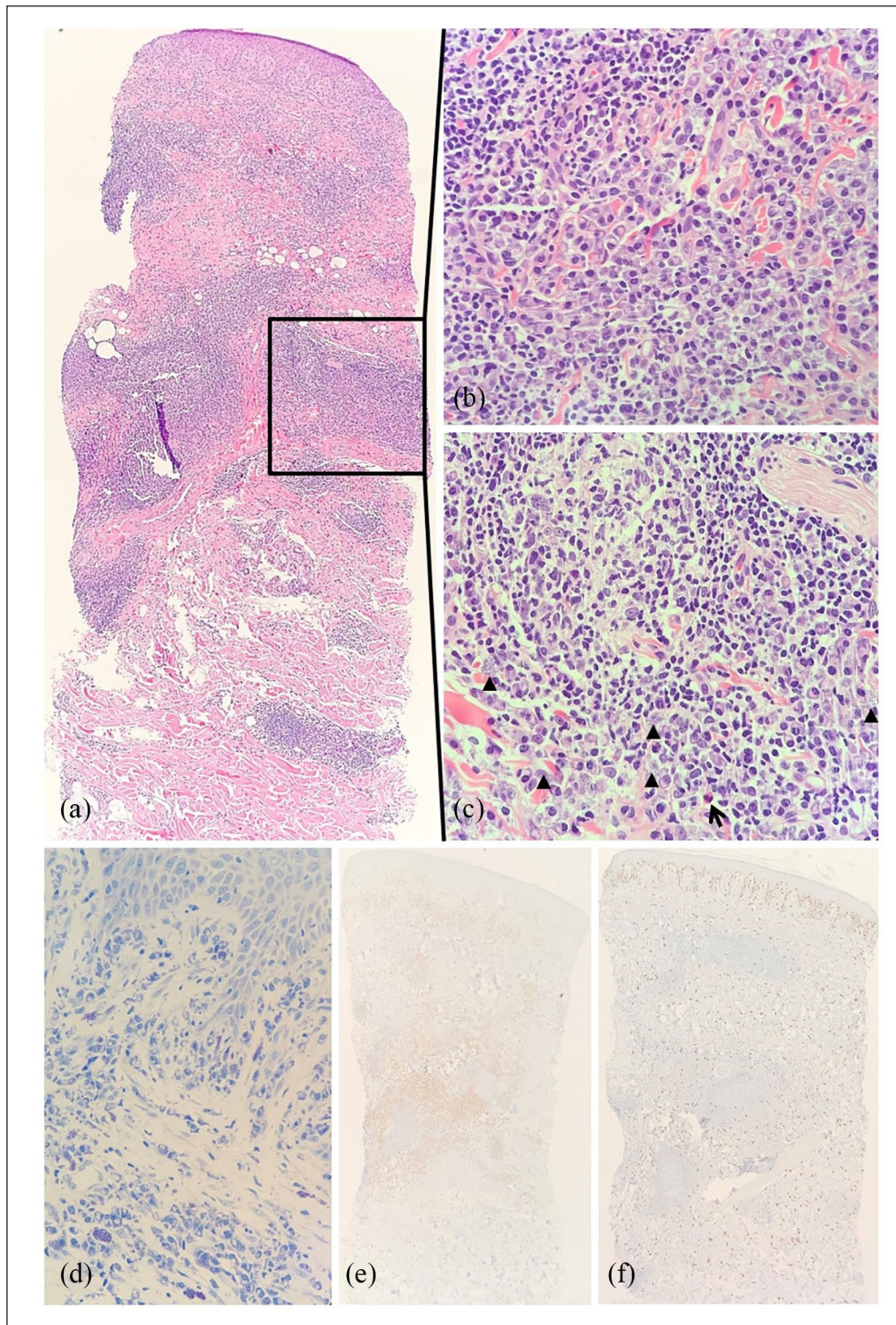
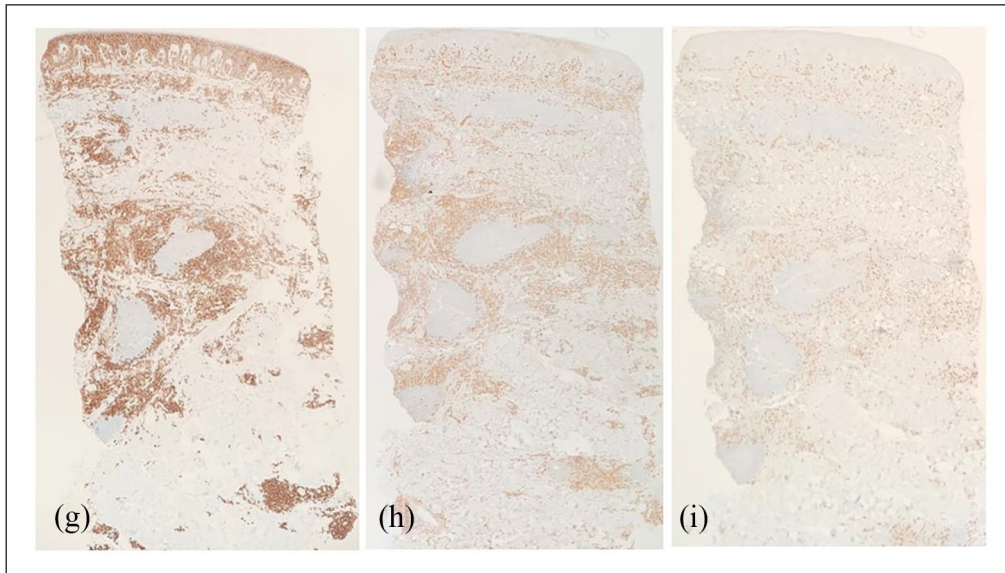
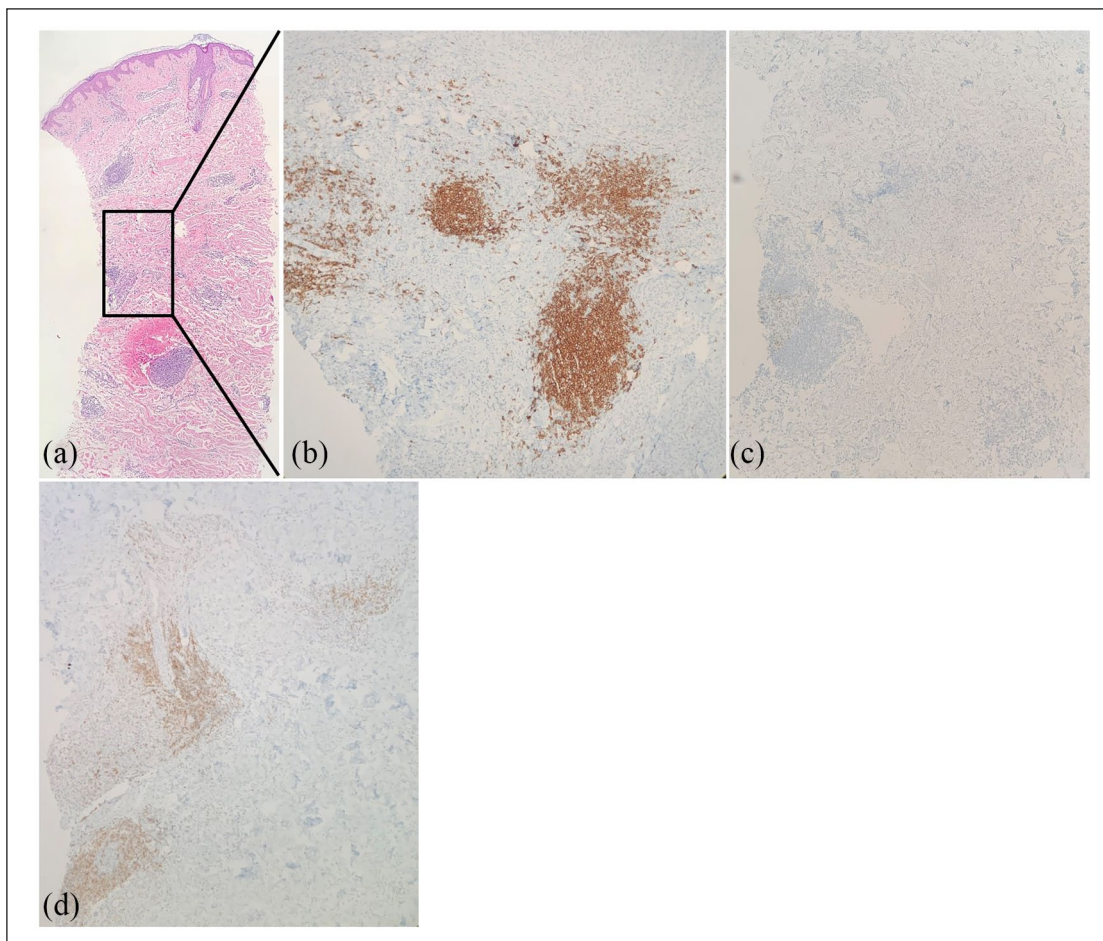


Figure 2. (Continued)



**Figure 2.** (a) Multiple, nodular infiltrates involving the reticular dermis, sparing the overlying epidermis (H&E,  $\times 40$ ). (b) Tumor cells, small to medium sized and having irregular nuclei, are present on the left of the field and plasma cells are seen in the center (H&E,  $\times 400$ ). (c) Scattered mast cells (arrowheads) and eosinophils (arrow) are found at the periphery of the infiltrate (H&E,  $\times 400$ ). (d, e) Mast cells are stained with toluidine blue and CD117 (toluidine blue, CD117,  $\times 400$ ). (f, g) Immunohistochemistry studies revealed multiple plasma cells (MUM1, CD138,  $\times 40$ ). Compared with the (h) lambda light chain, (i) kappa light chain is strongly expressed ( $\times 40$ ).



**Figure 3.** (a) Nodular infiltrates in the dermis (H&E,  $\times 40$ ). (b) Patchy positivity is shown (CD20,  $\times 100$ ). (c) Focal positive cells in the center of the follicle (BCL-6,  $\times 100$ ). (d) Numerous BCL-2 positive cells are present except in the small germinal center areas (BCL-2,  $\times 100$ ).

rare.<sup>6</sup> The pathology of PCMZL is still poorly understood; however, the origin appears to be multifactorial and its genesis probably involves chronic antigen stimulation. Recently, studies have suggested the existence of 2 subtypes of PCMZLs with differing histological, immunophenotypic, and microenvironmental features:<sup>7</sup> those with IgM expression (non-switched) and those with IgG expression (switched).<sup>1</sup> The majority express class-switched immunoglobulins and may arise in individuals with an allergic or atopic diathesis.<sup>6,7</sup> The less common subtype is IgM-positive and *Borrelia burgdorferi* antigen has been identified in this subtype from Europe but not in cases from the United States or Japan.<sup>7,8</sup> Usually, clinical manifestations consist of solitary lesion or clusters of asymptomatic, reddish brown to violaceous or purpuric papules, nodules, and plaques measuring from 1 to 10 cm in diameter. The trunk and arms are predominantly affected. Considering the clinical features, the diagnosis is established by skin biopsy, through histological and cytological examinations. Immunohistochemical and immunophenotypic, cytogenetic, and genotypic studies are also helpful in diagnosis.<sup>1</sup> In histological findings, PCMZL is typically characterized by a dense, lymphocytic infiltrate distributed mainly in the reticular dermis, and a Grenz zone can be found in most cases. Cytologically, it is composed of a polymorphous infiltrate that includes centrocyte-like, monocytoid, and lymphoplasmacytoid lymphocytes and plasma cells.<sup>2</sup>

As noted in our case, plasma cells can be the dominant cell component. Distinguishing marginal zone lymphoma (MZL) from other small B-cell lymphomas with plasmacytic differentiation, especially lymphoplasmacytic lymphoma, or from plasma cell neoplasms may be challenging.<sup>9</sup> Immunoglobulin heavy chain (IgH) gene rearrangements are used as molecular marker in approximately 80% of lymphoma and multiple myeloma (MM) patients since they represent lineage-specific markers. In addition, MM can be differentiated in that they exhibit a characteristic monoclonal immunoglobulin in immunofixation or immunoelectrophoresis of serum and urine. From a cytological viewpoint, neoplastic B cells resemble normal B cells that give rise to them, that is, monocytoid marginal zone B-cells and plasma cells in the case of PCMZL.<sup>1</sup> In the special stain, the CD20-positive reactive follicles showed BCL-2 positivity, and only the germinal center showed BCL-6 positivity, which also distinguished PCMZL from other PCBCLs.

One notable point was that multiple mast cells were observed in the specimen obtained from our patient. Clinically, it was possible to access the UP and evaluation of systemic mastocytosis was required. However, the patient had no accompanying systemic symptoms, and there was no indication of involvement of other organs in the examinations, including blood tests and peripheral blood smears. After treatment, the patient's symptoms also improved (Figure 1(c) and (d)), and as a result of consultation with a

hematology oncologist, further evaluation was decided to be withheld. Recent studies have demonstrated that mast cells serve as critical regulators of the tumor microenvironment,<sup>10</sup> enhance proliferation of B lymphocytes, and drive their differentiation toward IgA-secreting plasma cells. Eosinophils are present in about 25% of the cases and scattered mast cells may be prominent in PCMZL.<sup>11</sup> In 2010, Edinger et al.<sup>6</sup> identified prominent mast cells in PCMZL for the first time. It was reported that mast cells were observed in 13 class-switched cases and 3 non-switched cases and that the average number of mast cells was much higher in the class-switched cases. Tournilhac et al.<sup>12</sup> found that mast cells have been shown to be involved in B-cell survival and proliferation in lymphoplasmacytic lymphoma. Afterward, Rabenhorst et al.<sup>10</sup> found that PCBCL patients with a progressive course showed higher mast cell counts than stable patients and that mast cell counts were positively correlated with microvessel density.

However, PCMZL with prominent mastocytosis is very rare and there are not many reported cases. Much study is still needed on the role and relevance of mast cells in PCMZL, and it is meaningful that one reference is accumulated for future study by presenting this case. When diagnosing PCMZL, it is necessary to recognize once again that such a variety of cells can be seen and allow access to diagnosis through multidisciplinary evaluation. In this case, diffuse and abundant infiltration of mast cells was observed, which made the diagnosis more complicated. Therefore, this case is worth reporting for its rarity and for the purpose of reminding mastocytosis in PCMZL.

### Declaration of conflicting interests

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### Informed consent

Written informed consent was obtained from the patient prior to publication.

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