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CASE REPORT

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Primary cutaneous follicle center lymphoma with extensive plasmacytic differentiation and t(14;18) in both the lymphoid and plasma cell components

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Abstract

Primary cutaneous follicle center lymphoma (PCFCL) is the most common cutaneous B-cell lymphoma. The typical immunophenotype includes expression of both CD20 and BCL6, with the majority of cases lacking expression of CD10, BCL2, and the characteristic t(14;18)/*IGH-BCL2* rearrangement seen in systemic follicular lymphoma (FL). Plasmacytic differentiation (PD) is an uncommon finding in both systemic and cutaneous FLs and presents a diagnostic challenge when present, leading to the potential for misdiagnosis as marginal zone lymphoma (MZL). Limited reports have described light chain restriction in the plasma cell component of FLs with PD, and rare cases of PCFCL with PD have been described. While the *IGH-BCL2* translocation has been identified in a subset of FLs with PD, the presence of the *BCL2* translocation in monotypic plasma cells of PCFCL has not been previously described to our knowledge. Here, we report a case of PCFCL with extensive PD in a 77-year-old woman that was favored to represent primary cutaneous MZL on an initial punch biopsy. Excisional biopsy, however, revealed that the atypical lymphocytes expressed CD10, BCL6, and BCL2, while the plasma cell component demonstrated light-chain lambda restriction. FISH studies showed the presence of an *IGH-BCL2* translocation in both the lymphocytic and plasmacytic components.

KEYWORDS
cutaneous lymphomas, dermatopathology, hematopathology, in situ hybridization

1 | INTRODUCTION

Primary cutaneous lymphomas (PCLs) are non-Hodgkin lymphomas presenting in the skin without evidence of extracutaneous involvement at diagnosis. PCLs are distinguished from their systemic counterparts by different clinical presentation, treatment, and prognosis, as well as immunophenotypic and molecular features. Primary cutaneous follicle center lymphoma (PCFCL) is the most common primary cutaneous B-cell lymphoma and represents approximately 10% of cutaneous lymphomas.[1,2] The typical immunophenotype of PCFCL includes expression of B-cell markers such as CD19, CD20, and PAX5 as well as germinal center markers such as BCL6 and, less often, CD10.[2] The *IGH-BCL2* translocation is seen in a minority of cases (~10%-40%).[3-7] PCFCL must be distinguished from systemic follicular lymphoma (FL), which portends a significantly worse prognosis. PCFCL and FL show similar histopathologic features; however, FL usually shows strong expression of BCL2 and harbors t(14;18). Nonetheless, there is significant overlap between the morphology and immunophenotype of FL and PCFCL, and distinction between the two requires clinical correlation.

Here, we present a rare case of PCFCL with extensive plasmacytic differentiation (PD), mimicking primary cutaneous marginal zone lymphoma (PCMZL) on initial biopsy. As large clusters of

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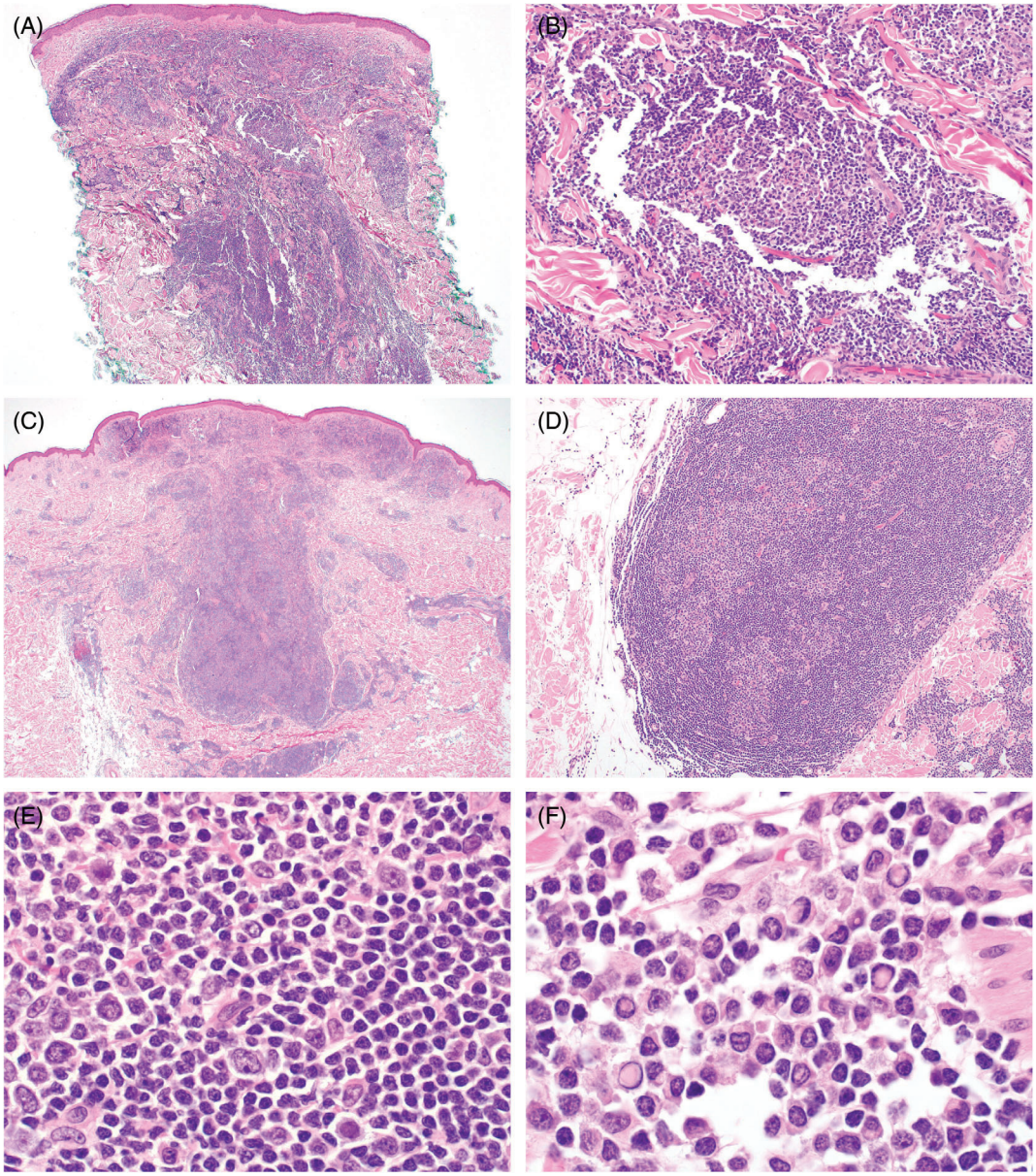


FIGURE 1 A, Initial punch biopsy specimen showing a dense pan-dermal infiltrate (H&E). B, Higher magnification reveals occasional small germinal centers among background small and medium-sized lymphocytes (H&E). Occasional plasma cells, some containing Dutcher bodies, were also present at the periphery of the infiltrate. C, Low-power image of the excision specimen showing a dense, vaguely nodular lymphoid infiltrate extending into the deep dermis (H&E). A grenz zone is present. D, The infiltrate contains numerous irregularly shaped lymphoid follicles lacking well-developed mantle zones (H&E). E, High-power image showing large lymphoid forms with vesicular chromatin and prominent nucleoli, consistent with centroblasts. Numerous smaller lymphocytes with condensed chromatin and irregular to cleaved nuclei, consistent with centrocytes, are intermixed (H&E). Tingible body macrophages are absent. F, At the periphery of the infiltrate are large clusters of plasmacytoid cells with conspicuous Dutcher bodies (H&E). Original magnification: A, ×40; B, ×200; C, ×20; D, ×100; E, ×600; F, ×1000

interfollicular neoplastic plasma cells (PC) were present, we performed fluorescence in situ hybridization (FISH) studies to reveal the presence of the *IGH-BCL2* fusion gene in both the lymphoid and plasmacytic components. A series of five cases of PCFCL with PD were recently reported; however, FISH studies for *BCL2* rearrangement were unable to be performed because of the small number of PC present and/or small sample size.[8] To our knowledge, this case adds the first report to the literature firmly demonstrating a clonal relationship between the plasmacytic and lymphoid components of a PCFCL with PD.

2 | CASE REPORT

A 77-year-old woman presented to her primary care physician with fluctuating pruritic papules on her right forearm that she attributed to arthropod bites. These papules persisted for a year and were refractory to medium- and strong-potency topical steroids. She otherwise remained asymptomatic with unremarkable laboratory values. Dermatologic evaluation revealed two 7-mm erythematous papules on her back with a clinical impression of persistent

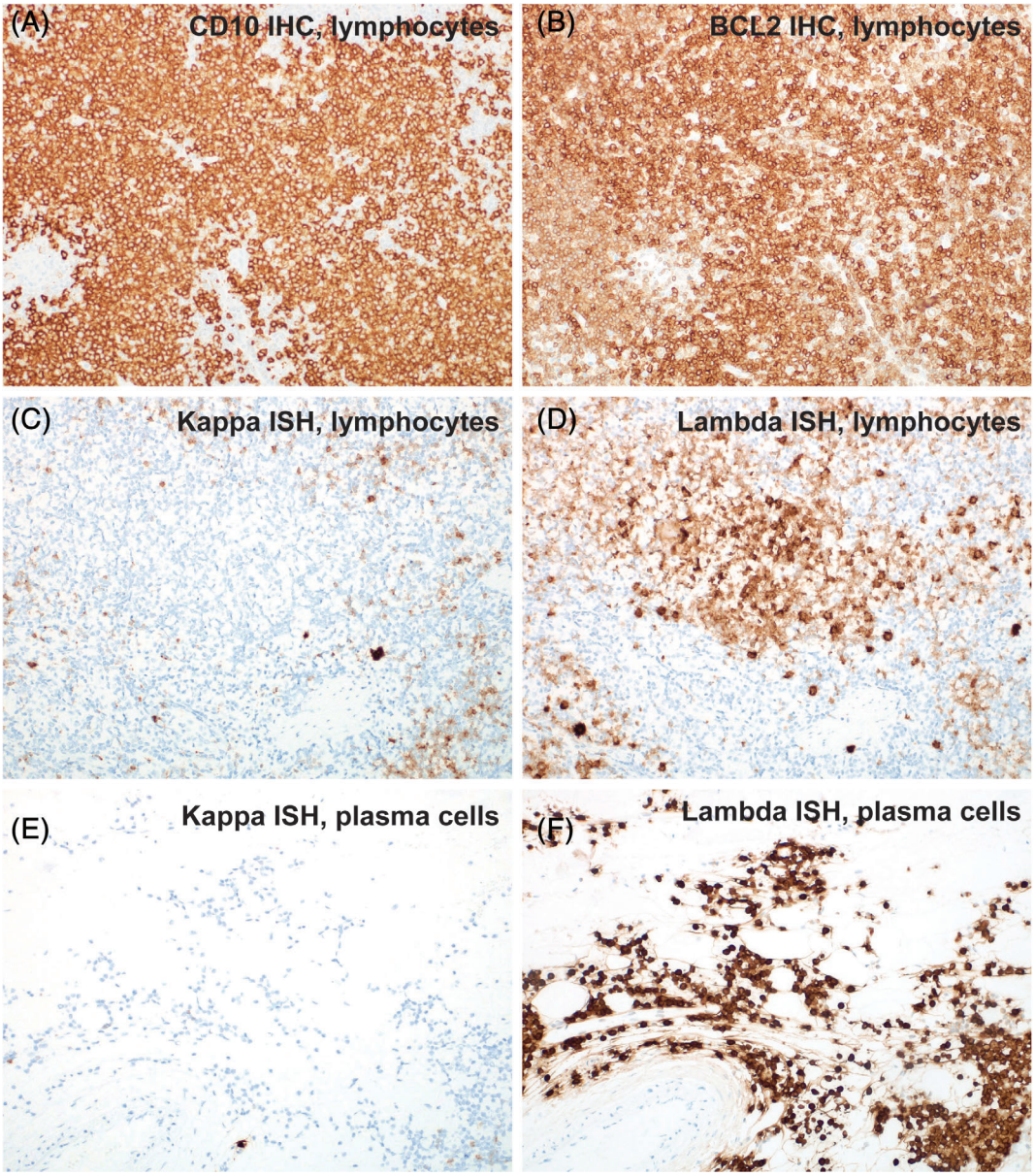


FIGURE 2 The neoplastic lymphocytes strongly express CD10 (A) and BCL2 (B) by immunohistochemistry. The neoplastic lymphocytes arranged in germinal centers show lambda light-chain restriction by in situ hybridization (ISH) with a polyclonal population of small lymphocytes in the background (C,D). The plasma cell (PC) population shows only scattered cells that are positive for immunoglobulin light chain kappa (E); however, most PCs express immunoglobulin light chain lambda (F) by ISH (lambda to kappa ratio > 10:1). Original magnification: A–F, ×200

arthropod bites vs reactive lymphoid hyperplasia ("pseudolymphoma") or lymphoma.

Initial small punch biopsy specimens showed a full-thickness dermal infiltrate of small- to medium-sized lymphocytes containing small germinal centers (Figure 1A,B). The infiltrate was favored to represent marginal zone lymphoma because of the presence of lambda-restricted PC with Dutcher bodies that were present predominantly at the periphery of the infiltrate. BCL6 highlighted germinal center B-cells, and CD21 highlighted loose follicular dendritic cell meshworks. Following this diagnosis, she was referred to hematology for staging evaluation including a computed tomography scan, which showed no evidence of systemic involvement. The patient followed with hematology every 6 to 12 months for approximately 4 years without progression until two new 1-cm papulonodules developed on her right scapula and within a scar on her left medial back.

Excisional biopsy of the new right scapular papule revealed a vaguely nodular dermal infiltrate of irregularly shaped germinal centers composed of a mixture of small- to medium-sized lymphocytes with irregular, cleaved nuclei (representing centrocytes) and large atypical lymphocytes with vesicular chromatin and prominent nucleoli (representing centroblasts; Figure 1C-E). Tingible body macrophages and well-developed mantle zones were absent. At the periphery were numerous PCs present in an interfollicular pattern. Compared to normal PC, the neoplastic PCs were slightly smaller in size with less cytoplasm and contained conspicuous Dutcher bodies (Figure 1F). Immunohistochemical studies highlighted a CD20-positive B-cell

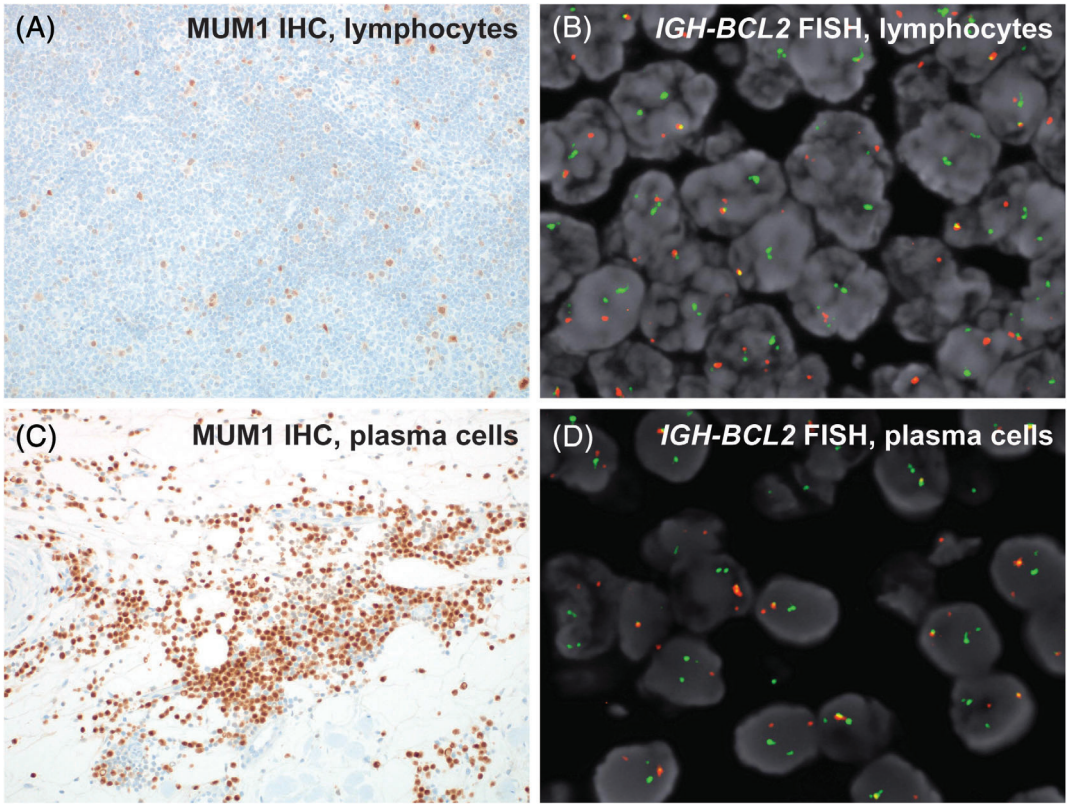


FIGURE 3 The lymphoid component, which lacks expression of MUM1 (A), shows evidence of the *IGH-BCL2* fusion gene in the majority of cells by dual-probe fluorescence in situ hybridization (B, yellow signal). The plasma cell component, which stains strongly and diffusely with MUM1 (C), also shows evidence of the *IGH-BCL2* rearrangement event in the majority of cells (D, yellow signal). Original magnification: A,C, ×200; B,D, ×1000; *IGH*, green; *BCL2*, orange; fusion, yellow

population strongly positive for CD10 (Figure 2A), BCL2 (Figure 2B), and BCL6, and negative for CD5, CD43, and cyclin D1. CD21 highlighted expanded follicular dendritic cell meshworks. Both the lymphoid and PC components showed immunoglobulin light-chain lambda restriction, the latter with a lambda to kappa ratio of >10:1 (Figure 2C-F). Overall, these findings were consistent with a follicle center B-cell lymphoma with extensive PD. Without evidence of systemic involvement, she was ultimately diagnosed with PCFCL.

The extensive PD in our case with areas at the periphery of the tumor composed almost exclusively of PCs provided the opportunity to investigate for *BCL2* rearrangement within the PC component. Dual-probe FISH for the t(14;18)/*IGH-BCL2* translocation was performed and revealed the presence of the fusion signal in a majority of cells within both the lymphoid (MUM1-negative) and plasmacytic (MUM1-positive) components (Figure 3).

3 | DISCUSSION

PCFCL and PCMZL are the most common CBCLs, accounting for approximately 50% and 35% of all CBCLs, respectively, and present a diagnostic challenge when PD is present.[8-11] This case illustrates the first report of a unique clinical and histopathologic presentation of a CD10-positive, BCL2-positive PCFCL with an extensive plasmacytic component demonstrating numerous Dutcher bodies, immunoglobulin light-chain lambda restriction, and *BCL2* translocation in both the lymphoid cells and PC. As in other reported cases, this example was favored to represent PCMZL on initial biopsy. Interestingly, the *IGH-BCL2* translocation has been reported in PCMZL, which is another potential source for diagnostic confusion.[12] Distinguishing PCMZL from PCFCL is important, as PCFCL has a somewhat lower 5-year survival.[2] Systemic FL has a substantially worse prognosis than MZL and requires exclusion in any case of follicle center B-cell lymphoma presenting in the skin, particularly those that show BCL2 expression and harbor t(14;18).

PCFCLs are classically single or localized lesions on the head, neck, or trunk in middle-aged and older individuals. Untreated, the lesions gradually increase in size and may be locally aggressive or show extracutaneous spread.[2,13-15] Treatment may include observation, excision, and/or local radiation. Rituximab may also be added in cases with extensive skin involvement, while chemotherapy is reserved for marked skin involvement or extracutaneous spread. The prognosis is excellent with a 5-year survival of 95%, which is unaffected by grade, growth pattern, BCL2 expression, the presence of t(14;18), extent, or relapse of disease.[1,3-5,16]

Immunophenotypically, the neoplastic lymphocytes of PCFCL are in most cases positive for BCL6 and less commonly CD10, most often without expression of BCL2.[1,4,5,17] If present, BCL2 is usually at most

dim and patchy in only 20% to 40% of cases,[3,4] but has been reported in up to 86% of cases.[5,6] Rare cases can even demonstrate strong positivity for BCL2.[6] Additionally, the characteristic t(14;18)/*IGH-BCL2* rearrangement seen in systemic follicular lymphoma is not classically seen in PCFCL,[18] but can be present in about 10% to 40% of PCFCLs,[3-6] and is more likely present when both CD10 and BCL2 are positive by immunohistochemistry (IHC).[4,5] Light-chain restriction is not commonly seen in small B-cell lymphomas (SBCLs) because of low expression of immunoglobulins by lymphocytes, and is most likely identified by routine IHC in PC when present.[19,20]

PD can be seen in nearly all SBCLs to a variable extent[9,11] and has rarely been reported in FL.[10,11,21-24] In both systemic and cutaneous forms, PCs, including those with Dutcher bodies or with Mott cell morphology, are significantly more common in MZLs than in follicle center B-cell lymphomas. All small B-cell lymphomas are thought to be arrested at a particular stage of development; PCFCL is arrested at the germinal center stage, whereas MZLs have arrested after germinal center selection. The maturation arrest of follicle center lymphomas is likely multifactorial; however, expression of CD10, BCL2, and BCL6 may be involved.[11,25,26] PD in follicle center B-cell lymphomas has been divided into two morphologic types with one type having predominately interfollicular PC, usually with *BCL2* rearrangement, and the second type having predominately intrafollicular/perifollicular PC, usually without *BCL2* rearrangement in either component.[10,17] PD in PCFCL is particularly rare with only limited reports in the literature. A series of five cutaneous FLs (four of which represented PCFCL) with PD was recently reported.[8] In this series, only one case had a prominent PC component (present in up to 50% of the follicles), while the other four cases showed only scattered or individual PC. As PCs were largely intermixed with lymphocytes and/or biopsies were small, FISH studies to detect the *BCL2-IGH* translocation in this population could not be interpreted. Interestingly, none of the cases had Dutcher bodies or Mott cells. A retrospective review by the European Association for Haematopathology/Society for Hematopathology further emphasizes the rarity of marked PD in FLs and found only one case of a systemic plasmacytic FL with Dutcher bodies and Mott cells.[11] No other cases of Dutcher bodies or Mott cells in PCFCL have been reported in the literature.

Here, we add to the literature one additional diagnostically challenging case of PCFCL with extensive PD and evidence of the *IGH-BCL2* translocation in both the lymphocytic and PC components. To our knowledge, *BCL2* rearrangement in the monotypic PC component of PCFCL with PD has not been previously described. In addition, this case further supports the association of PC distribution (interfollicular vs intrafollicular/perifollicular) with respect to *BCL2* translocation status that has been well described in systemic FL.

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CONFLICT OF INTEREST

The authors report no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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