

CASE REPORT

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Soft tissue sarcoma unmasked: An atypical presentation of primary cutaneous B-cell lymphoma

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ABSTRACT

Introduction: Primary cutaneous follicle center lymphoma (PCFCL) is the most common subtype of primary cutaneous B-cell lymphoma and is typically an indolent malignancy with an excellent prognosis. However, atypical presentations may mimic soft tissue sarcoma or high-grade lymphoma, creating significant diagnostic challenges.

Case Report: In this report, we describe a unique case of a young male with a history of systemic lupus erythematosus (SLE) who presented with a slowly enlarging, ulcerated soft-tissue mass of the lower back with associated drainage, pain, fever, and weight prompting treatment with dose-adjusted R-EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab) loss. Upon admission, cross-sectional imaging and fluorine-18 fluorodeoxyglucose (18F-FDG) positron emission tomography–computed tomography (PET-CT) revealed a large (15 cm) right dorsal soft tissue mass with intense FDG uptake. Core needle biopsy initially demonstrated a high-grade

appearing B-cell lymphoma with a concern for high grade lymphoma. Following additional immunostaining and multidisciplinary hematopathology review, the diagnosis was revised to PCFCL with a diffuse growth pattern. The patient completed four cycles of inpatient chemotherapy with a reduction in mass size after each cycle.

Conclusion: Here we present a case of PCFCL with a diffuse growth pattern that mimicked both soft-tissue sarcoma and high-grade B-cell lymphoma, highlighting the importance of prompt tissue diagnosis and comprehensive pathologic evaluation.

Keywords: Diffuse growth pattern, Primary cutaneous B-cell lymphoma, Primary cutaneous follicle center lymphoma, Soft tissue mass, Soft tissue sarcoma

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INTRODUCTION

Non-Hodgkin lymphoma (NHL) accounts for approximately 90% of all lymphomas and encompasses a group of lymphoid tissue malignancies that arise due to clonal expansion of B cells, T cells, or natural killer cells [1, 2]. Although B-cell non-Hodgkin lymphoma (B-NHL) is common and represents 95% of all NHL, primary extra-nodal NHL makes up less than one-third of all patients [3]. Furthermore, cutaneous lymphoma involvement is much more likely to be of T cell origin (70–80%) as opposed to B cell type (20–30%) [4–6]. Primary

cutaneous B cell lymphoma (PCBCL) is diagnosed in approximately 0.5–1 case per 100,000 people each year, with the most common subclassifications being primary cutaneous marginal zone lymphoma, primary cutaneous follicle center lymphoma (PCFCL), or diffuse large B-cell lymphoma, leg type (pcDLBCL) [7–10].

Primary cutaneous follicle center lymphoma (PCFCL) is the most common PCBCL and makes up roughly 10% of all cutaneous lymphomas [11]. It is generally considered to be an indolent lymphoma with an excellent prognosis and is associated with a 5-year disease-specific survival $\geq 95\%$ [12]. Primary cutaneous follicle center lymphoma typically presents as solitary or grouped pink–purple papules, plaques, or nodules on the head, neck, or trunk. Lesions typically do not exceed 3 cm in diameter and demonstrate slow, progressive growth without treatment. Patients are usually asymptomatic, and ulceration is rare [13].

Herein, we present a unique case of PCFCL with a diffuse growth pattern and a high proliferative index, mimicking high-grade lymphoma, which was diagnosed following core needle biopsy of what was initially thought to be tumid lupus erythematosus or soft tissue sarcoma (STS).

CASE REPORT

A 54-year-old Jamaican male with a past medical history of diabetes mellitus, rheumatoid arthritis, and systemic lupus erythematosus (SLE) presented to the emergency department of a safety-net hospital for evaluation of a several-year history of a slowly enlarging, ulcerated soft tissue mass of the lower back with numerous associated smaller cutaneous nodules. He had a three-month history of new onset drainage and pain at the mass, in addition to recent fever, chills, generalized malaise, and 20-pound weight loss. Several of the lesions were stable for years and then became ulcerated approximately eight months prior to presentation. Initial workup in Jamaica, three months prior to presentation at our institution, included a tissue biopsy of the mass. Pathology review at the outside institution was most consistent with tumid lupus erythematosus, prompting initiation of methotrexate 2.5 mg weekly and hydroxychloroquine 400 mg daily, with recommendation for surgical resection.

Due to limited local resources, the patient sought care in the United States for further workup and management. No changes to the mass were noted after initiation of the disease-modifying antirheumatic drugs, and the wound was being managed with daily local wound care. He had no known personal or family history of malignancy.

Upon presentation to our institution, the surgical oncology and dermatology services were consulted. Physical examination was notable for an approximately 15 cm, mildly tender, firm, partially necrotic soft tissue mass of the right flank with an open, draining wound containing fibrinous exudate and several surrounding smaller cutaneous nodules (Figure 1A–C). Workup included cross-sectional imaging and serologic testing to evaluate

possible infectious, autoimmune, and hematologic causes of the lesion. This included QuantiFERON-Gold testing for tuberculosis, rapid plasma reagin (RPR) for syphilis, human immunodeficiency virus (HIV) testing, blood cultures, and hepatitis B and C serologies. Tuberculosis screening was included because cutaneous tuberculosis can present with nodular or plaque-like lesions that may mimic lymphoproliferative disorders or soft tissue tumors. All infectious studies were negative. Given the patient's history of SLE, antinuclear antibody (ANA) testing was also obtained to evaluate for autoimmune disease activity. Specifically, lupus panniculitis, reported in approximately 1–3% of patients with SLE, can present with deep subcutaneous nodules that clinically resemble subcutaneous lymphoma or soft tissue tumors. Antinuclear antibody testing was negative. Epstein–Barr virus (EBV) testing and glucose-6-phosphate dehydrogenase (G6PD) testing to evaluate lymphoproliferative or hematologic processes, respectively, were both unremarkable.

Computed tomography scan of the abdomen and pelvis with intravenous (IV) contrast revealed a large, 15 cm $\times$ 12 cm heterogenous ulcerated right dorsal soft tissue mass with internal gas and non-enhancing components with no associated fluid collections (Figure 2). Initial findings were most concerning for a malignant process, specifically STS given the rapid rate of tumor progression and necrosis. The patient then proceeded to a core needle biopsy with expedited pathologic evaluation due to inability to obtain previous pathology records. Pathologic evaluation demonstrated medium to large sized CD20+ B cells diffusely infiltrating the soft tissue (Figure 3). The neoplastic population also expressed the germinal center marker CD10, with weak BCL2 co-expression, and demonstrated a very high Ki-67 proliferative index of greater than 95% (Figure 3B). The infiltrate was negative for terminal deoxynucleotidyl transferase (TdT) and cyclin D1. These results established the diagnosis of a B cell lymphoma with a concern for a high-grade lymphoma, as from the pathologic standpoint, it was unclear if there was involvement beyond the initial presentation of large cutaneous and subcutaneous masses. Fluorescence In Situ Hybridization (FISH) analysis was negative for MYC, BCL2, and/or BCL6 rearrangements. To prioritize tissue for FISH analysis, Epstein–Barr Encoded RNA (EBER) in situ hybridization was not initially performed on the core biopsy sample.

The Hematology Oncology service was consulted for further management. Positron emission tomography–computed tomography showed intense FDG uptake in the mass, focal intense uptake in a region of small nodularity in the left upper back likely representative of a site of tumor involvement, and a small soft tissue density in the right upper chest wall with hypermetabolic activity concerning for possible lymphomatous involvement. Magnetic resonance imaging of the spine and CT of the chest did not demonstrate any additional sites of further disease involvement.

Due to the large size of the mass and the initial concern for an aggressive B-cell lymphoma with high-grade features, initiation of treatment with

chemoimmunotherapy with dose adjusted EPOCH-R (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab) for six cycles for curative intent was recommended to the patient.

Additional pathology review and immunostaining revealed BCL6 positivity, EBER ISH and MUM1 negativity, and confirmation of the lack of CD21+ follicular dendritic meshworks, which together with the integration of additional clinical information that the disease was confined to the skin upon clinical staging, supported a final diagnosis of PCFCL with a diffuse growth pattern.

At this time, the patient has tolerated and completed four of six recommended cycles of inpatient systemic chemotherapy. Since initiation of therapy, the large mass on his back has almost entirely clinically responded (Figure 4A–D). He will continue to follow up with the oncology team for completion of planned systemic chemotherapy.



Figure 1: Initial presentation of ulcerated, necrotic, draining soft tissue mass. (A, B) Large necrotic and ulcerating mass along the right thoracic and lumbar region measuring approximately 20 cm at time of presentation to safety-net hospital. (C) Multiple painless, non-ulcerated irregular nodules on upper back bilaterally without surrounding erythema or drainage.



Figure 2: Cross-sectional imaging with CT of the abdomen and pelvis was performed following intravenous injection of 85 mL iohexol (Omnipaque 350 mg/mL) and demonstrated a large, ulcerated right dorsal soft tissue mass measuring approximately 14.5 cm x 7.7 cm x 12.1 cm at time of presentation to safety-net hospital.

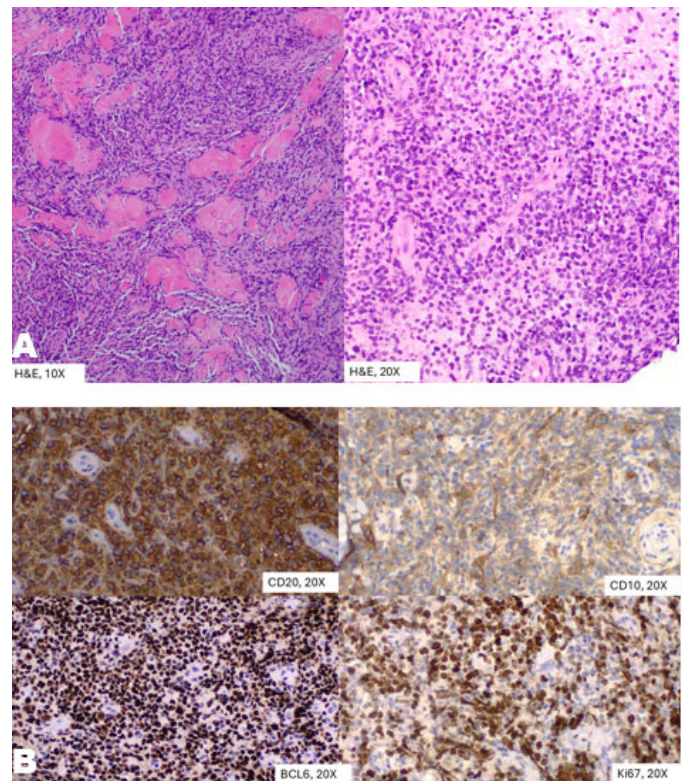


Figure 3: Histopathologic evaluation of right flank mass. (A) Hematoxylin and eosin (H&E) staining at low ($\times 10$) and higher ($\times 20$) magnification demonstrating a malignant lymphomatous infiltrate with a diffuse growth pattern. (B) Immunohistochemical staining demonstrating that the neoplastic lymphoma cells exhibit positivity for CD20, CD10, and BCL6 with a markedly elevated Ki-67 proliferation index ($>95\%$).



Figure 4: Progressive response of soft tissue mass with subsequent chemotherapy cycles (A) after receipt of the first cycle of DA-R-EPOCH therapy, (B) on day of receipt of second cycle of DA-R-EPOCH therapy, (C) on day of receipt of third cycle of DA-R-EPOCH therapy, and (D) near resolution of right flank soft tissue mass after receipt of fourth cycle of DA-R-EPOCH therapy.

DISCUSSION

Primary cutaneous follicle center lymphoma is the most common subtype of PCBCCL in Caucasians, accounting for 30–50% of all PCBCCL cases, while it is the least common subtype in Asian countries like Japan and Korea. It predominantly affects males with a median age at onset in the fifth to sixth decades of life [13]. Multifocal skin involvement occurs in only 10–15% of cases and does not carry prognostic significance, and dissemination to extracutaneous sites is rare. Atypical presentations have been described and can pose a diagnostic challenge, as PCFCL may mimic inflammatory conditions such as lupus tumidus, granulomatous rosacea, and IgG4-related disease, as well as solid organ metastasis or other cutaneous neoplasms [13]. Given this broad differential, tuberculosis screening was also included in our patient's evaluation, as cutaneous tuberculosis can present with nodular or plaque-like lesions that may mimic lymphoproliferative disorders or soft tissue tumors [14, 15].

In this case, the patient presented with a rapidly enlarging 15 × 12 cm ulcerated dorsal soft tissue mass with radiographic findings initially concerning for STS, given the rapid rate of tumor progression and necrosis [16, 17]. Histopathologic evaluation established the diagnosis of B cell lymphoma rather than STS, demonstrating a diffuse growth pattern and markedly elevated Ki-67 proliferative index (95–100%), features more commonly associated with aggressive B-cell lymphomas [18]. This patient's lymphoma cells were also positive for BCL2, a finding more common in primary cutaneous large B cell lymphoma, leg type (PCLBCL-LT). However, our patient's lymphoma cells were also CD10 positive, a finding not usually seen in PCLBCL-LT, lacked the typical PCLBCL-LT morphology of confluent sheets of centroblasts and/or immunoblast-like large cells, and also lacked the strong BCL2 and MUM1 expression that characterizes PCLBCL-LT. Although PCFCLs usually lack BCL-2 expression and BCL2 gene rearrangement, BCL-2 can be expressed, usually weakly, in a subset of PCFCL cases. In addition, elevated Ki-67 proliferative indexes may be seen in PCFCL with a diffuse growth pattern [19]. Thus, primary cutaneous B-cell lymphomas require a multiparametric approach and careful clinicopathologic correlation to overcome diagnostic challenges [13].

As per National Comprehensive Cancer Network (NCCN) guidelines, recommended workup for PCFCL includes biopsy with comprehensive immunophenotypic characterization demonstrating expression of B-cell markers (CD20, CD79a, and BCL6), assessment of CD10 and BCL2 expression, clinicopathologic correlation, and appropriate staging studies to exclude systemic involvement [20]. In our patient, additional immunostaining demonstrated BCL6 positivity, MUM1 negativity, EBER ISH negativity, and lack of CD21+ follicular dendritic meshworks, with multidisciplinary review at hematopathology consensus conference ultimately supporting a diagnosis of PCFCL [21].

Primary cutaneous follicle center lymphoma can exhibit three histologic growth patterns: follicular, mixed follicular-diffuse, and diffuse. The diffuse variant may be particularly challenging to recognize because it lacks the well-formed follicular structures typically associated with follicle center lymphomas and can therefore resemble more aggressive cutaneous B-cell lymphomas [22]. Notably, these histologic patterns do not independently affect prognosis. Outcomes in PCFCL remain favorable across all growth patterns, with a 5-year disease-specific survival of 95% that is unaffected by grade, BCL2 expression, t(14;18) status, disease extent, or relapse [23].

Although he received a previous diagnosis of tumid lupus, this was discordant with his presentation at our safety-net hospital. While oral and nasal ulcers are well-documented mucocutaneous manifestations of SLE and are included in the current classification criteria, cutaneous ulcers, particularly those on the trunk, are relatively uncommon and typically occur only in the context of lupus-associated vasculitis or advanced systemic disease [24, 25]. Lupus Erythematosus Panniculitis is a separate disease that can also overlap with SLE and rarely presents with ulcerations. Specifically, lupus panniculitis, reported in approximately 1–3% of patients with SLE, can present with deep subcutaneous nodules that clinically resemble subcutaneous lymphoma or soft tissue tumors [26]. However, it usually presents in areas of increased fat deposition, such as the arms and legs (gluteal region and thighs) and face, not the back like in this case, further supporting our patient's discordant presentation with SLE [24].

Contrastingly, this patient's clinical presentation was more consistent with, and initially presumed to be, STS due to its rapid progression, recurrence following drainage, and areas of necrosis [16, 17]. STS often presents as a painless, progressively enlarging mass, with high-grade lesions typically growing over weeks to months. Approximately 60% of soft tissue sarcomas arise in the extremities [16]. Atypical variants of PCFCL can exhibit sarcomatous morphology that closely mimics soft-tissue neoplasms [27]. Our patient's unique situation, with lack of access to prior records and concern for rapid disease progression, necessitated expedited biopsy. This deviation from typical workup allowed for prompt histopathologic diagnosis and the early initiation of inpatient chemotherapy, emphasizing the importance of maintaining a broad differential diagnosis and considering cutaneous manifestations of disease processes like lymphoma.

Treatment of PCFCL is generally stage-dependent and reflects its indolent clinical behavior. For patients with localized disease, the NCCN recommends involved-site radiation therapy as the preferred initial treatment, achieving complete remission rates approaching 100% [20]. In select patients, observation, surgical excision, skin-directed therapies, or intralesional corticosteroids may also be considered [20]. Multi-agent chemoimmunotherapy is typically reserved for patients

with extensive, refractory, or extracutaneous disease because of associated toxicity [13].

In contrast, our patient underwent treatment with dose-adjusted R-EPOCH rather than conventional skin-directed therapy. At the time treatment was initiated, PET imaging was interpreted as being consistent with stage IV disease with a dominant cutaneous lesion and possible nodal involvement. Coupled with the preliminary diagnosis of high-grade B-cell lymphoma and a markedly elevated Ki-67 proliferative index (95–100%), these findings prompted the decision to initiate systemic dose-adjusted R-EPOCH. While formal restaging imaging has not yet been performed, the mass has shown substantial clinical improvement, with noticeable reduction in size after each chemotherapy cycle, indicating a favorable early response to treatment (Figure 4A–D).

CONCLUSION

Herein, we present a patient with an atypical presentation of PCFCL with a diffuse growth pattern that was initially mistaken for STS and tumid lupus erythematosus. Prompt tissue biopsy, comprehensive immunophenotypic evaluation, and multidisciplinary clinicopathologic review were essential in establishing the correct diagnosis and guiding appropriate treatment, resulting in near-complete resolution of the primary lesion. This case highlights the importance of maintaining a broad differential diagnosis and pursuing timely tissue diagnosis and clinicopathologic correlation when evaluating atypical cutaneous or soft tissue masses.

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Author Contributions

Paridhi Agarwal – Conception of the work, Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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