

Rare Cutaneous Presentation of Burkitt Lymphoma

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PRACTICE POINTS

- Cutaneous metastasis is exceedingly rare in Burkitt lymphoma. When cutaneous involvement does occur, it can represent an uncommon consequence of a surgical procedure, serving as the inciting event for hematogenous spread and local tumor extension into the skin.
- Although cutaneous metastasis of Burkitt lymphoma typically is associated with high disease burden and mortality, our case demonstrated that cutaneous spread can be present even in a patient who has a positive outcome. Our patient was able to achieve disease remission and complete resolution of cutaneous lesions with continued chemotherapy, suggesting that cutaneous metastasis does not always portend a poor prognosis.

To the Editor:

A 73-year-old man was admitted to the hospital with progressive abdominal and hip pain of several weeks' duration that was accompanied by unilateral swelling of the left leg. He had a medical history of hypertension, hyperlipidemia, and prediabetes. Computed tomography (CT) showed extensive intra-abdominal, retroperitoneal, and pelvic lymphadenopathy in addition to poorly defined hepatic lesions.

A CT-guided core biopsy of a left inguinal lymph node showed Burkitt lymphoma. Fluorescence in situ hybridization was positive for oncogene *c-MYC* rearrangement on chromosome 8q24 and negative for B-cell lymphoma 2 (*BCL2*) and B-cell lymphoma 6 (*BCL6*)

gene rearrangements. Flow cytometry demonstrated an aberrant population of κ light chain-restricted CD5⁻CD10⁺ B lymphocytes.

The patient's overall disease burden was consistent with stage IV Burkitt lymphoma. R-miniCHOP chemotherapy—rituximab plus a reduced dose of cyclophosphamide, doxorubicin, vincristine sulfate, and prednisone—was initiated. Approximately 2 weeks after chemotherapy was initiated, the patient developed a firm erythematous eruption on the left hip (Figure 1A). His regimen was then switched to R-EPOCH—rituximab, etoposide phosphate, prednisone, vincristine sulfate, cyclophosphamide, and doxorubicin—at the time of discharge, and he was referred to dermatology due to an initial concern of an adverse reaction to R-EPOCH chemotherapy. The patient denied any pain, pruritus, or irritation. Physical examination showed multifocal, subcutaneous, indurated, erythematous and violaceous nodules without epidermal changes. Some nodules on the lateral aspect of the hip coalesced to form firm plaques.

A punch biopsy specimen showed markedly atypical lymphocytes with enlarged nuclei and scant cytoplasm present throughout the dermis (Figures 2A and 2B). Numerous apoptotic cells and cellular debris were seen. Immunohistochemical staining demonstrated that the lymphocytic infiltrate comprised CD79a⁺ B cells that were positive for Bcl-6 and CD10 and negative for Bcl-2 (Figures 2C and 2D). There also was diminished focal expression of CD20. Ki-67 protein staining was intensely positive and demonstrated a very high proliferative index.

Taken together, these findings were consistent with a diagnosis of cutaneous metastasis of Burkitt lymphoma. The patient's cutaneous lesions improved after continued

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FIGURE 1. A, Erythematous and violaceous indurated nodules and plaques on the left lower abdomen and left hip that were later diagnosed as cutaneous Burkitt lymphoma. B, Regression of lesions was noted after the second round of R-EPOCH chemotherapy—rituximab, etoposide phosphate, prednisone, vincristine sulfate, cyclophosphamide, and doxorubicin.

aggressive chemotherapy. At follow-up 2 weeks after biopsy, he was receiving his second round of R-EPOCH chemotherapy with appreciable regression of skin lesions (Figure 1B). However, he then developed right-side double vision, ptosis, and right-side facial paresthesia. Although magnetic resonance imaging of the brain and lumbar puncture did not show evidence of central nervous system involvement, the chemotherapy regimen was switched to dose-adjusted CVAD-R—hypercyclophosphamide, vincristine, doxorubicin hydrochloride, and dexamethasone plus rituximab—for empiric treatment of central nervous system disease. Although treatment was complicated by sepsis with extended-spectrum β -lactamase-producing *Enterobacter cloacae*, Burkitt lymphoma was found to be in remission after 3 cycles of CVAD-R and 5 months of chemotherapy.

Burkitt lymphoma is a B-cell non-Hodgkin malignancy caused by translocation of chromosome 8 and chromosome 14, leading to overexpression of *c-MYC* and subsequent hyperproliferation of B lymphocytes.^{1,2} The disease is divided into 3 major categories: sporadic, endemic, and immunodeficiency related.³ The endemic variant is the most prevalent subtype in Africa and is associated with *Plasmodium falciparum* malaria; the sporadic variant is the most common subtype in the rest of the world.⁴

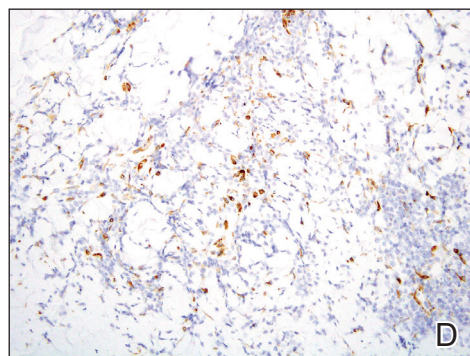
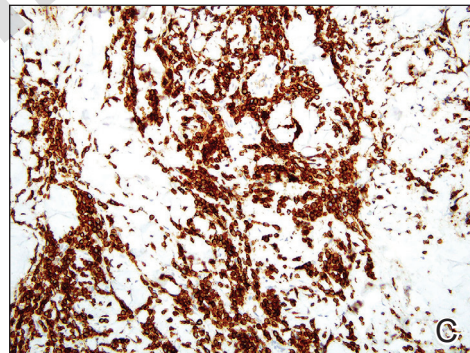
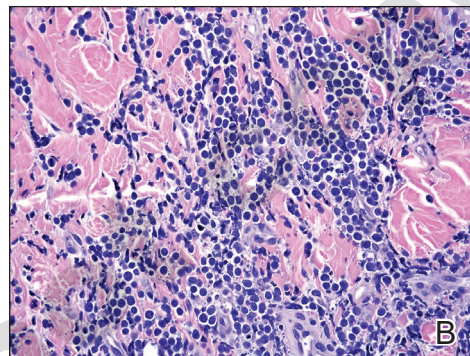
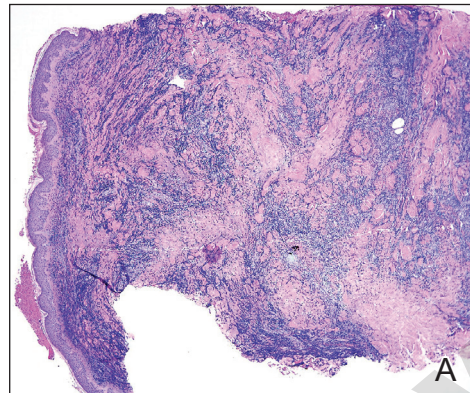


FIGURE 2. A and B, A punch biopsy specimen showed markedly atypical lymphocytes present throughout the dermis (H&E, original magnifications $\times 4$ and $\times 40$). Lymphocytes have enlarged nuclei and scant cytoplasm. Numerous apoptotic cells with cellular debris were present. C and D, Immunohistochemical staining demonstrated that the infiltrate was comprised of CD79a⁺ B cells that were Bcl-6 positive (original magnifications $\times 20$), respectively.

Burkitt lymphoma is highly aggressive and is characterized by unusually high rates of mitosis and apoptosis that result in abundant cellular debris and a distinctive starry-sky pattern on histopathology.^{5,6} Extranodal metastasis is common,⁷ but cutaneous involvement is exceedingly rare, with only a few cases having been reported.⁸⁻¹⁴ Cutaneous metastasis of Burkitt lymphoma often is associated with a high overall disease burden and poor prognosis.^{8,11}

Immunodeficiency-related Burkitt lymphoma is particularly aggressive. Notably, 3 of 7 (42.9%) reported cases of cutaneous Burkitt lymphoma occurred in HIV-positive patients.^{11,13} In one case, cutaneous involvement was the first sign of relapsed disease that had been in remission.¹²

Although c-MYC rearrangement is required to make a diagnosis of Burkitt lymphoma, the disease also is present in a minority of cases of diffuse large B-cell lymphoma (DLBCL)(6%).¹⁵ Although DLBCL typically can be differentiated from Burkitt lymphoma by the large nuclear size and characteristic vesicular nuclei of B cells, few cases of DLBCL with c-MYC rearrangement histologically mimic Burkitt lymphoma. However, key features such as immunohistochemical staining for Bcl-2 and CD10 can be used to distinguish these 2 entities.¹⁶ Bcl-2 negativity and CD10 positivity, as seen in our patient, is considered more characteristic of Burkitt lymphoma. This staining pattern in combination with a high Ki-67 fraction (>95%) and the presence of monomorphic medium-sized cells is more consistent with a diagnosis of Burkitt lymphoma than of DLBCL.¹⁷

Earlier case reports have documented that cutaneous lesions of Burkitt lymphoma can occur in a variety of ways. Hematogenous spread is the likely route of metastasis for lesions distant to the primary site or those that have widespread distribution.¹⁸ Alternatively, other reports have suggested that cutaneous metastases can occur from local invasion and subcutaneous extension of malignant cells after a surgical procedure.^{10,19} For example, cutaneous Burkitt lymphoma has been reported in the setting of celioscopy, occurring directly at the surgical site.¹⁹ In our patient, we believe that the route of metastatic spread likely was through subcutaneous invasion secondary to CT-guided core biopsy, which was supported by the observation that the onset of cutaneous manifestations was temporally related to the procedure and that the lesions occurred on the skin directly overlying the biopsy site.

In conclusion, we describe an exceedingly rare presentation of cutaneous Burkitt lymphoma in which a surgical procedure likely served as an inciting event that triggered seeding of malignant cells to the skin. Cutaneous spread of Burkitt lymphoma is infrequently reported; all such reports that provide long-term follow-up data have described it in association with high disease burden and often a lethal outcome.^{8,11,12} Our patient had complete resolution of cutaneous lesions with chemotherapy. It is unclear if the presence of cutaneous lesions can serve as a prognostic indicator and requires further investigation.

However, our case provides preliminary evidence to suggest that cutaneous metastases do not always represent aggressive disease and that cutaneous lesions may respond well to chemotherapy.

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