# Primary Skeletal Muscle Lymphoma Presenting as Refractory Cellulitis

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*The right torso of a 55-year-old woman showed diffuse skin and soft-tissue changes suggestive of cellulitis. However, several clinical and radiologic features, including the subacute and nontoxic nature of the illness and the patient's lack of response to antibiotic therapy, indicated a noninfectious etiology. Malignancy was suggested by striking changes seen on computed tomographic scanning—including extensive infiltration and enlargement of the musculature of the right shoulder girdle, the intercostal musculature, the latissimus dorsi, and the rhomboids; focal enlargement of the right paraspinal muscles; and enlargement of the psoas and the iliacus muscles and of the musculature around the hip joint. The mediastinal, hilar, and paraaortic regions showed no adenopathy. A large hypodense lesion of approximately 4.5 cm, which was seen in the caudate lobe of the liver, raised the concern of a metastatic focus of malignancy. Because of these findings, an immediate muscle biopsy was performed. Results showed a non-Hodgkin's lymphoma with a B-cell phenotype. Although primary skeletal muscle lymphoma is very uncommon in patients without human immunodeficiency virus infection, clinical presentation of refractory cellulitis, as seen in the current case, is extremely rare.*

Involvement of primary skeletal muscle in non-Hodgkin's lymphoma is extremely rare among patients without human immunodeficiency virus infection. For example, a recent review of 33 years of English literature revealed only 31 cases of primary skeletal muscle lymphoma.[1] A localized mass, often in an extremity, was a frequent presentation. To our knowledge, primary skeletal muscle lymphoma has never presented as a refractory cellulitislike syndrome. Therefore, we provide the following case report as the first description of non-Hodgkin's lymphoma with primary skeletal muscle involvement presenting as cellulitis refractory to antibiotic therapy.

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## Case Report

A 55-year-old woman presented to her primary care physician and complained of painful, erythematous, and indurated skin changes of approximately 6 weeks' duration. Initially, the physician noted skin changes at the right flank; later, they involved the skin and soft tissues of the right hip, the right lateral breast and axilla, and the right scapular region. In addition, the patient described right-side lumbar back pain that had been present for several months. During this time, she had no high fever or chills, but she experienced decreased appetite, malaise, and low-grade (<100°F) fever. The patient had lost 20 pounds over the preceding 3 months and had a past history of hypertension and cigarette smoking.

Physical examination showed marked skin and soft-tissue changes extending from the right scapular and lateral chest areas caudally to the right lateral hip (Figure 1). The skin changes included erythema and induration, which was suggestive of cellulitis. However, the patient was afebrile and nontoxic in appearance. No adenopathy or hepatosplenomegaly was noted. Despite a course of parenteral and then oral antibiotics for treatment of presumed cellulitis, the skin and soft-tissue changes and the right-side flank and lower back pain persisted.

Subsequent computed tomographic (CT) scanning showed extensive infiltration and enlargement of the musculature of the right shoulder girdle, the intercostal musculature, the latissimus

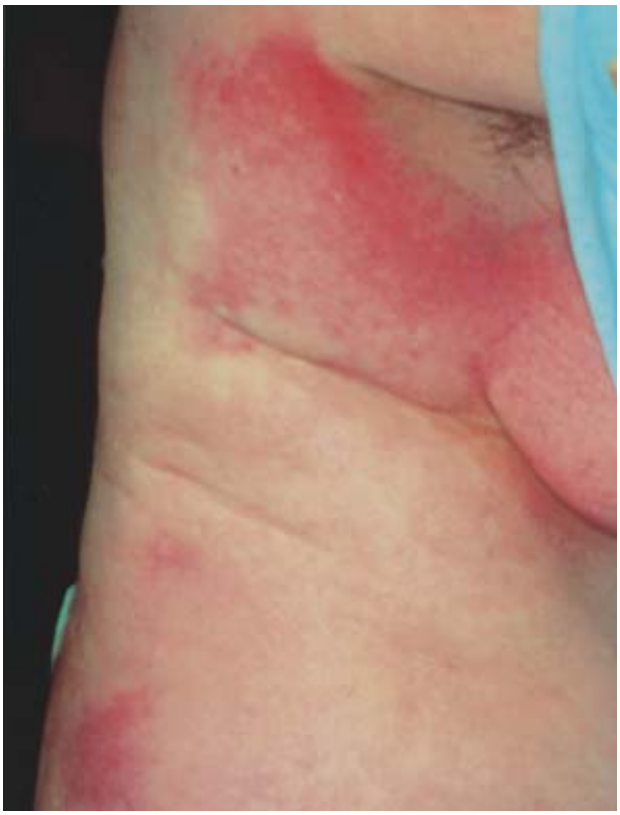

**Figure 1.** Extensive erythema and induration on the right torso.

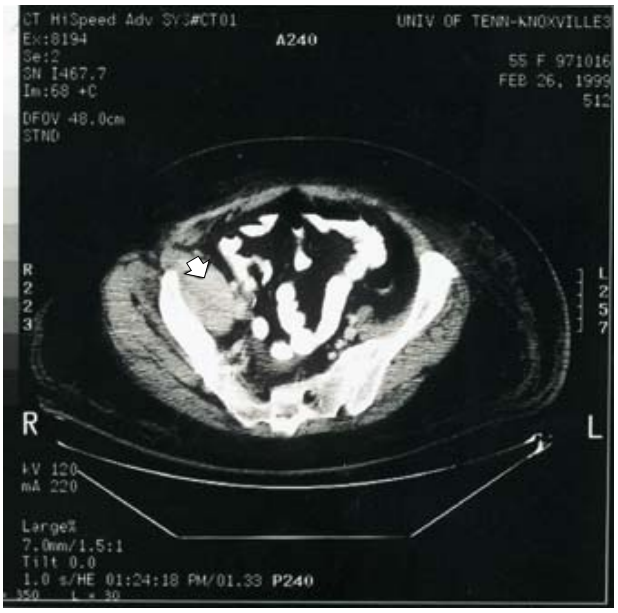


**Figure 2.** Axial computed tomographic scan shows enlargement of right iliacus muscle (arrowhead).

dorsi, and the rhomboids; focal enlargement of the right paraspinal muscles; and enlargement of the psoas and the iliacus muscles (Figure 2) and of the musculature around the hip joint. There was a medium-sized pleural effusion on the right but no mediastinal or hilar adenopathy. A large hypodense lesion of approximately 4.5 cm was present in the caudate lobe of the liver, but no paraaortic adenopathy was seen. Thus, an open skin-and-muscle biopsy of the right posterior scapular region was done.

Routine hematoxylin and eosin (H&E) stains of microscopic sections showed an aggressive malignancy composed of small-to-medium lymphoid cells admixed with a subset of larger cells (Figure 3, A and B). The tumor cell nuclei had coarse clumped chromatin and irregular nuclear contours; the larger cell nuclei contained small nucleoli. Tumor cells extended from deep skeletal muscle and infiltrated subcutaneous tissues up to the superficial dermis. The epidermis was uninvolved. Striated muscle fibers and adipose tissue were completely obliterated by sheets of malignant cells. Mitotic activity and apoptosis were brisk, with numerous atypical mitotic forms present. Immunohistochemical studies performed on paraffin-embedded tissue showed that the neoplastic cells stained positively with CD20 antigen (Figure 4), indicating B-cell origin, and expressed a monotypic κ light-chain restriction. No gene rearrangements were identified on submitted fresh-frozen tissue. Flow-cytometric evaluation of fresh tissue showed a reactive T-cell population that, on flow-diagram review, was not perceived to represent the malignant cell population. Lack of B cells, highlighted by flow-cytometric evaluation, was likely either due to tissue sampling or lack of CD45 antigen expression on cell membranes. Therefore, the tumor was classified as a diffuse large–B-cell lymphoma.

After bone-marrow examination, which showed no malignant involvement, chemotherapy was initiated with doxorubicin, vincristine, and high-dose dexamethasone. Treatment led to resolution of cutaneous changes and pain and dramatic improvement in CT scan findings. Human immunodeficiency virus–antibody screening performed during this time was negative.

## Comment

Local cutaneous changes, including erythema, have been described in only 2 patients with primary skeletal muscle lymphoma.[2,3] One patient was initially thought to have deep-vein thrombophlebitis.[2] Local physical examination findings included marked swelling, induration, and erythema of the left thigh. Initial therapy included heparin and then warfarin sodium, but the local thigh changes persisted. Subsequent evaluation with a CT scan showed massive

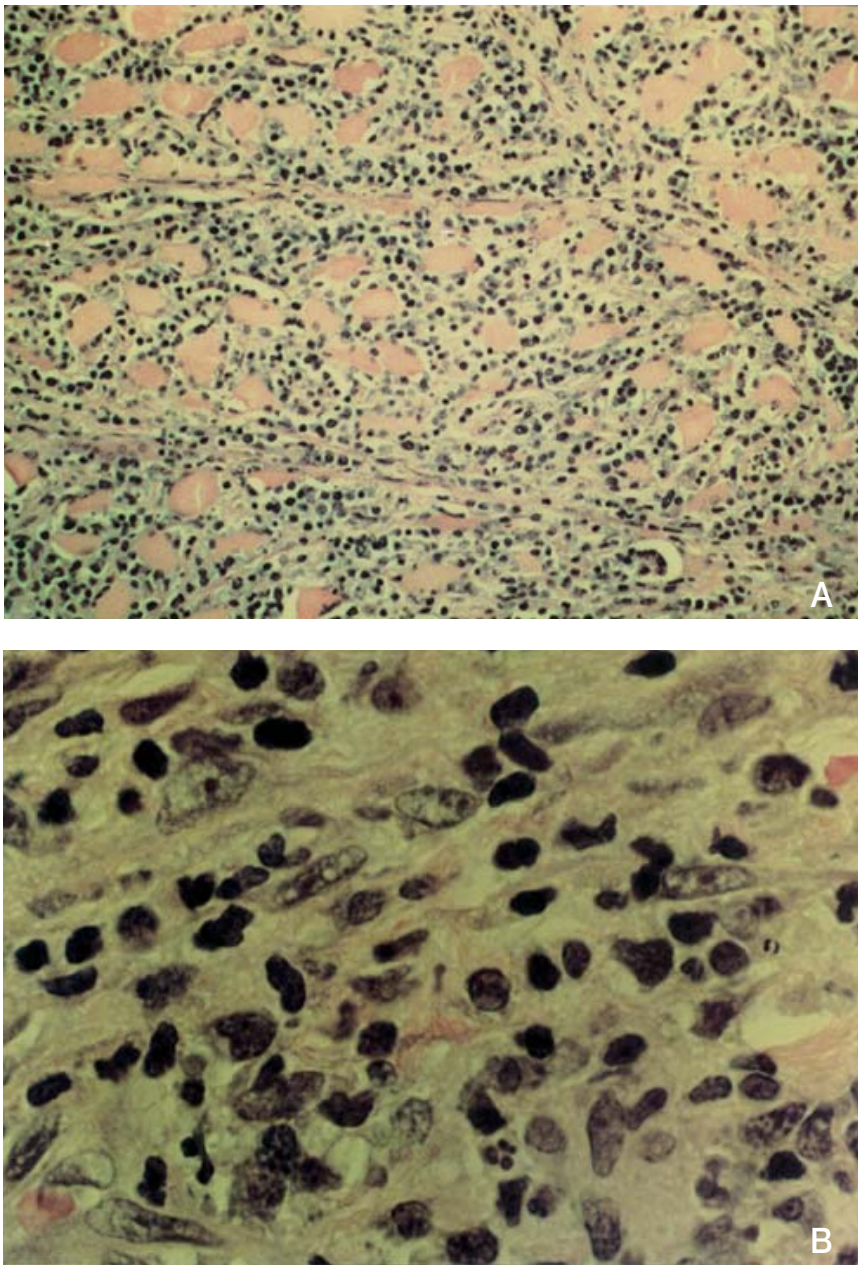


**Figure 3.** (A) A right posterior scapular muscle biopsy showing extensive infiltration with sheets of malignant cells and degenerated skeletal muscle fibers and obliteration of adipose tissue (H&E, original magnification ×200). (B) Admixture of small-to-medium and large cells (H&E, original magnification ×1000).

enlargement of the left quadriceps muscle. Muscle biopsy revealed a malignant large-cell lymphoma. The other patient had a 10-week history of a painful enlarging mass on the right thigh and erythema that was warm to the touch on initial physical examination.[3] Biopsy of the mass showed lymphoma.

The pathogenic mechanisms involved in the production of skin erythema in patients with primary skeletal muscle lymphoma are undefined. In the case reported here, skin biopsy showed malignant cells infiltrating the superficial dermis. Immune or inflammatory mediators are possibly key factors in the production of local skin changes, but the presence of these factors was not examined in this case. Another possibility is that secondary cellulitis due to bacterial infection causes such changes in the presence of local lymphatic and venous compromise[4] produced by the infiltrating tumor. However, the subacute and nontoxic characteristics of the patient's presentation, the lack of response to antibiotics, and the response to cancer chemotherapy all support a lymphomatous etiology of the cellulitislike syndrome.

The extent of tumor involvement in the current case was also unusual among reported cases of primary skeletal muscle lymphoma. In previous reports of patients presenting with local mass

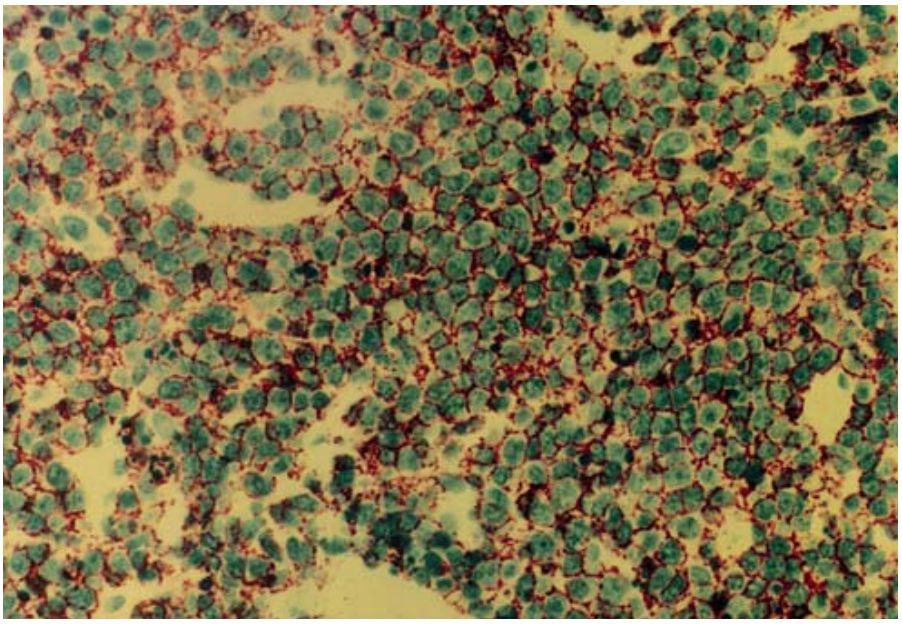

**Figure 4.** Paraffin-embedded tissue (CD20 antigen immunoperoxidase, original magnification ×400).

lesions, lymphoma typically was localized at the time of diagnosis to one muscle group, usually involving an extremity.[1-3,5] In reviewing the literature, Chim et al[1] summarized the histopathologic findings of 31 cases of primary skeletal muscle lymphoma. These lymphomas typically have high-grade histology and tend to be of B-cell origin. Immunohistochemical studies showed that 30 of the 31 cases reviewed by Chim et al were of B-cell lineage. Chong et al[5] described 2 cases of extranodal non-Hodgkin's B-cell lymphoma involving the muscles of mastication. One case was diffuse large-cell lymphoma; the other was diffuse, small-lymphocytic, plasmacytoid lymphoma.

Definitive diagnosis of primary skeletal muscle lymphoma, a rare entity, requires routine histologic examination, immunohistochemical studies, and correlation with radiographic imaging studies to rule out a nodal connection with secondary involvement of muscle. Our case indicates the need to include lymphoma in the differential diagnosis of refractory cellulitis. The treatment approach is typically based on the histologic features of the tumor.

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