An adolescent with granulomatous mycosis fungoides infiltrating skeletal muscle successfully treated with oral prednisone

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INTRODUCTION

Mycosis fungoides (MF) is a T-cell lymphoma that originates in the skin and can spread to lymph nodes and the blood or even visceral organs in later stages of the disease.1 MF involvement of skeletal muscle, however, is extremely rare, having only been reported in 4 patients.2-5 We describe a 14-year-old boy with granulomatous MF (GMF) that infiltrated his left thigh muscles and responded to high-dose oral prednisone. To our knowledge, he represents the first reported case of MF with muscle involvement exhibiting a response to therapy.

CASE REPORT

We previously reported the case of a 14-year-old white boy with GMF,6 a variant of MF rarely seen in pediatric patients. In September 2015, he presented with 34.5% body surface area (BSA) involvement, and stage IB disease was diagnosed after studies showed no evidence of systemic disease. The subsequent biopsy results and clinical course contribute substantial information to the original report.

After his diagnosis, the patient received triamcinolone, clobetasol, and ultraviolet B phototherapy 3 times per week, resulting in a decrease from 34.5% to 9% of his affected BSA in February 2016. He continued to respond well to this regimen until June 2016, when he was hospitalized for a 10-day history of tenderness in his left inner thigh. Examination found an area of rock-hard induration that was not present previously. Laboratory findings were significant for a creatinine level of 3.23 mg/dL.

Fig 1. An atypical lymphoid infiltrate with admixed multinucleated histiocytes infiltrating surrounding fibroconnective tissue and skeletal muscle. (Hematoxylin-eosin stain; original magnification: ×20).

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calcium level of 14.7 mg/dL, and uric acid level of 8.9 mg/dL, indicative of acute kidney injury, calcinosis, and hyperuricemia. Renal biopsy found changes consistent with analgesic nephropathy.

Needle core biopsy of the left thigh found an atypical lymphohistiocytic infiltrate consisting of predominantly small lymphocytes with hyperchromatic nuclei and irregular nuclear contours admixed with numerous histiocytes, multinucleated giant cells, and rare eosinophils. The infiltrate involved the fibroconnective tissue and infiltrated skeletal muscle fibers, consistent with GMF with muscular infiltration (Fig 1). High-throughput sequencing of T-cell receptor CDR3 performed at Adaptive Biotechnologies found multiple dominant sequences in the T-cell receptor-β and T-cell receptor-γ genes shared across the patient’s skin, muscle, and blood samples, providing support for a common clonal T-cell process. Moreover, a positron emission tomography/computed tomography (PET/CT) scan showed increased subcutaneous soft tissue thickening and hypermetabolism (standardized uptake value, 4.4–12.7) of the left thigh muscles, left gastrocnemius, right tibialis anterior, bilateral foot muscles, and right scrotum, among other areas (Fig 2, A).

All topical therapies and phototherapy were discontinued. The pediatric oncology team considered use of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) but agreed to proceed with conservative management. He was started on oral prednisone, 30 mg, and allopurinol, 200 mg daily, and discharged from the hospital 7 days later. In July 2016, he reported significant
improvement in his skin lesions and his left thigh mass. Cutaneous examination found no induration of his left medial thigh and an affected BSA that had decreased to 3%. A PET/CT scan without contrast showed disease improvement in the subcutaneous tissues and musculature of all affected areas in the lower extremities (Fig 2, B). Prednisone was continued for 1 month given his clinical improvement, although he did experience steroid-induced acne and diabetes mellitus managed with insulin. In August 2016, his prednisone dose was tapered to 5 mg daily, topical steroids were resumed, and bexarotene gel was prescribed to help prevent development of granulomatous slack skin.

At his most recent follow-up visit in November 2016, his creatinine level had improved to 1.62 mg/dL, his uric acid level had returned to within normal limits, and his steroid-induced acne and diabetes had resolved (hemoglobin A1C level of 6.2%). Allopurinol was discontinued, but he remains on low-dose prednisone and insulin. Examination found MF patch involvement of 9.3% of his total BSA with expected erythema secondary to use of bexarotene gel.

**DISCUSSION**

MF is an extranodal, non-Hodgkin lymphoma of CD4+ T cells that originates in the skin and classically may progress through or present with 3 types of skin lesions: patch, plaque, and tumor. Involvement of extracutaneous sites such as lymph nodes, the blood, and visceral organs may occur in later stages and indicates more aggressive disease. Lymph nodes are the most common extracutaneous site affected, followed by the lung, spleen, and liver.

Skeletal muscle involvement in lymphoma is rare (1.8%) and is extraordinarily rare in MF. Epstein et al. found that 6 of 86 (7.0%) MF patients showed muscle involvement on autopsy. However, only 4 cases are reported in antemortem patients (Table I). Of these, only 1 case is described in a patient who, like ours, had GMF. In addition, although MF involving usual sites typically occurs in cases of blood involvement or large cell transformation, only one of the reported patients exhibited advanced disease, and none showed evidence of large cell transformation. The site of involvement in all 4 cases was the gastrocnemius muscle, which was also affected in our patient, although not the primary site. To our knowledge, our case is the only muscular infiltration of MF diagnosed in a pediatric patient.

It is known that GMF indicates aggressive disease and confers a poor prognosis. The effect of muscular infiltration on prognosis, however, remains unclear given its rarity, but it likely portends a poor

### Table I. Characteristics of patients with MF involving skeletal muscle

| No. | Reference | Age at onset (year) | Sex | Age at diagnosis (year) | Stage | GMF | Muscle(s) involved | Muscle MF treatment | Muscle MF involvement | Status/survival |
|-----|-----------|--------------------|-----|------------------------|-------|-----|-------------------|--------------------|---------------------|---------------|
| 1   | Shigeno et al (1982) | F | 67 | 84 | III/IV | n | Gastrocnemius | Unknown | Died of pneumonia 6 weeks after muscle involvement | Died of pneumonia 6 weeks after muscle involvement |
| 2   | Machler et al (1994) | F | 54 | 12 | IA/B | y | Gastrocnemius | Oral bexarotene, IFN-α, oral isotretinoin, PUVA, topical steroids | Localized radiation (27 Gy) | Minimal response; died of sepsis 3 months after muscle involvement |
| 3   | Hazrati et al (2007) | F | 12 | 20 | IA/B | y | Gastrocnemius | Oral bexarotene, IFN-α, PUVA, topical steroids, radiation | Rapid deterioration; palliative care started at age 22 | Rapid deterioration; palliative care started at age 22 |
| 4   | Weishaupt et al (2011) | M | 16 | 25 | IA/B | n | Gastrocnemius | PEG IFN-α, PUVA, topical steroids, UVB | Oral bexarotene, IFN-α | Partial response |
| 5   | Current case | M | 11 | 14 | IA | y | Feet, gastrocnemius, thigh, tibialis anterior | Topical bexarotene, oral steroids | Partial response | Partial response |

Gy, Gray; IFN, interferon; n, no; PEG, pegylated; UVB, ultraviolet B; PUVA, psoralen plus ultraviolet A; y, yes.
prognosis, as since it represents stage IVB disease. After all, 3 of the 4 patients in the literature died shortly from aggressive disease after diagnosis of muscle involvement, including the patient with GMF. Only one reported patient was able to maintain stable disease with treatment. However, none of these patients received systemic steroids, which resulted in a significant response in our patient. Because he is the first patient to exhibit a response to therapy, administration of high-dose systemic steroids may represent a reasonable therapeutic approach for MF infiltrating skeletal muscle.

As in the reported cases, our patient showed a neoplastic T-cell infiltrate in the epidermis penetrating the dermis and subcutis as well as the underlying muscle. It has been speculated that the malignant lymphocytes in MF are attracted to musculature and skin similar to the lymphocytes observed in dermatomyositis. In fact, in 1 of the 4 cases, a gallium citrate (67-Ga) scan showed increased muscle uptake, which has also been reported to occur in dermatomyositis. The reason for this musculotropism remains unclear, and further analysis of homing markers in musculocutaneous lymphocytic infiltrates remains a topic of future study.

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