Pediatric Acral Site Cutaneous T-Cell Lymphoma Imitating Acromegaly

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abstract

Cutaneous T-cell lymphoma (CTCL) is an infrequent non-Hodgkin lymphoma of the skin, with mycosis fungoides (MF) as the most common subtype. MF in palms and soles is an exceptionally rare presentation, particularly in pediatric patients. We report a case of a 17-year-old boy presenting with progressive enlargement of his hands and feet with thickening of palms and soles, initially suspected to have acromegaly. Laboratory and imaging workup ruled out endocrine and genetic causes of acromegaly. A skin biopsy confirmed a diagnosis of MF. This case illustrates the diagnostic challenges of pediatric MF, due to both its extreme rarity and potential for overlapping clinical presentation with other systemic conditions. The patient's socioeconomic background and immigration status limited initial access to specialized care, further complicating the evaluation and underscoring the health care barriers for immigrant populations. Community health centers play a crucial role in early diagnosis and care coordination, yet limited access to dermatology services in rural areas remains a significant challenge. Beyond expanding our current understanding of pediatric MF and broadening the differential diagnosis of acral enlargement in adolescents, this case emphasizes the importance of equitable health care access for immigrant patients. The findings highlight the need for increased dermatologic services in community health settings and among underserved populations.

INTRODUCTION

Cutaneous T-cell lymphoma (CTCL) is a heterogeneous group of non-Hodgkin lymphomas characterized by clonal T-cell proliferation in the skin.[1] Currently, the World Health Organization (WHO) acknowledges 10 subtypes of CTCL; the most common is mycosis fungoides (MF).[2] MF is a chronic, indolent disease that progresses through patch, plaque, and tumor stages, typically appearing on sun-protected areas such as the trunk or proximal extremities.[3] The patch and plaque stages of MF can resemble many dermatoses in the erythematous, hyperpigmented, or hypopigmented families, earning it the title of "the great imitator."[4] Though not a WHO-recognized CTCL subtype, a rare presentation of hyperkeratotic plaques or patches in the palms and soles has been described, known as mycosis fungoides palmaris et plantaris (MFPP).[5] Notably, pediatric CTCL is uncommon.[6] And pediatric MFPP is exceptionally so.[5]

The evaluation of CTCL should include a thorough clinical examination and a full-thickness skin biopsy, which includes immunohistochemical analysis to assess T-cell markers. Additionally, performing T-cell receptor gene rearrangement studies can further assist in confirming clonality.[7] Treatment depends on disease stage, with early-stage disease managed with topical therapies, phototherapy, or localized radiation and advanced or refractory disease requiring systemic therapies, including retinoids, interferons, or chemotherapy.[8] Acral sites pose treatment

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Dr Zha conceived, drafted, critically reviewed, revised, and supervised the manuscript edits. Mr Ding carried out the background literature review and critically reviewed and revised the manuscript. Dr Cheeney collected histopathological data and critically reviewed and revised the manuscript. Dr Felt collected clinical data and approved the final version. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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challenges with topical medications due to their thicker skin and anatomical constraints. For this reason, psoralen plus UVA (PUVA) is potentially more effective given its deeper skin penetration.[9] However, because increased epidermal melanin can act as a natural UV filter, reducing the penetration of UVA light into the skin,[10] PUVA may be less effective in treating CTCL in skin of color.[9]

We present a rare case of pediatric acral presentation of MF involving all 4 distal extremities resembling acromegaly (Figure 1). In addition to the extraordinarily rare presentation, the patient's unique socioeconomic situation and immigration status posed significant diagnostic and treatment challenges. These increasingly relevant issues highlight the critical roles community physicians play in advocacy and equity.

CASE PRESENTATION

A 17-year-old boy presented to the pediatric clinic at a rural community health center with a 9-year history of expanding hypopigmented rash, which started on his back and eventually extended to his extremities. This was followed by a 4-year history of gradually worsening "swelling" of hands and feet. Neither the rash nor the acral enlargement was associated with pruritus or pain. The patient's main concern was having difficulty finding shoes that fit, which limited his ability to run. The patient had no significant past medical history and was not taking any medications or supplements. Additionally, he was a recent immigrant from Mexico and spoke only Spanish. Though no medical records were available, the patient reported no relevant family history.

Upon presentation, the patient had normal vital signs and growth parameters. Physical examination revealed striking enlargement of the hands and feet, particularly in the palmar aspects. Pes planus was noted due to significant soft tissue thickening. The toes were sausage-like, with dystrophic or absent nails on some digits (Figure 1). Further inspection revealed subtly erythematous plaques with areas of hyperpigmentation, hypopigmentation, and lichenification on the proximal arms, axillae, flank, shoulders, and posterior knees (Figure 2). There were no signs of gigantism, excessive sweating, seborrhea, acanthosis nigricans, facial changes, macroglossia, voice changes, musculoskeletal symptoms, erythroderma, lymphadenopathy, or any metabolic or systemic signs.

The initial differential diagnoses were acromegaly, hypothyroidism, chromosomal disorders such as Klinefelter syndrome or X-linked acrogigantism, and tumor-related conditions like pituitary hyperplasia. Initial workup showed normal complete blood count, comprehensive metabolic panel, urinalysis, lactate dehydrogenase, thyrotropin, free thyroxine, antinuclear antibody, creatine kinase, erythrocyte sedimentation rate, and C-reactive protein. Subsequent tests, including insulin-like growth factor binding protein 3, insulin-like growth factor I, testosterone, prolactin, and chromosomal analysis, were also normal. Radiographs of the hands and feet revealed moderate generalized nonspecific soft tissue swelling but no bony

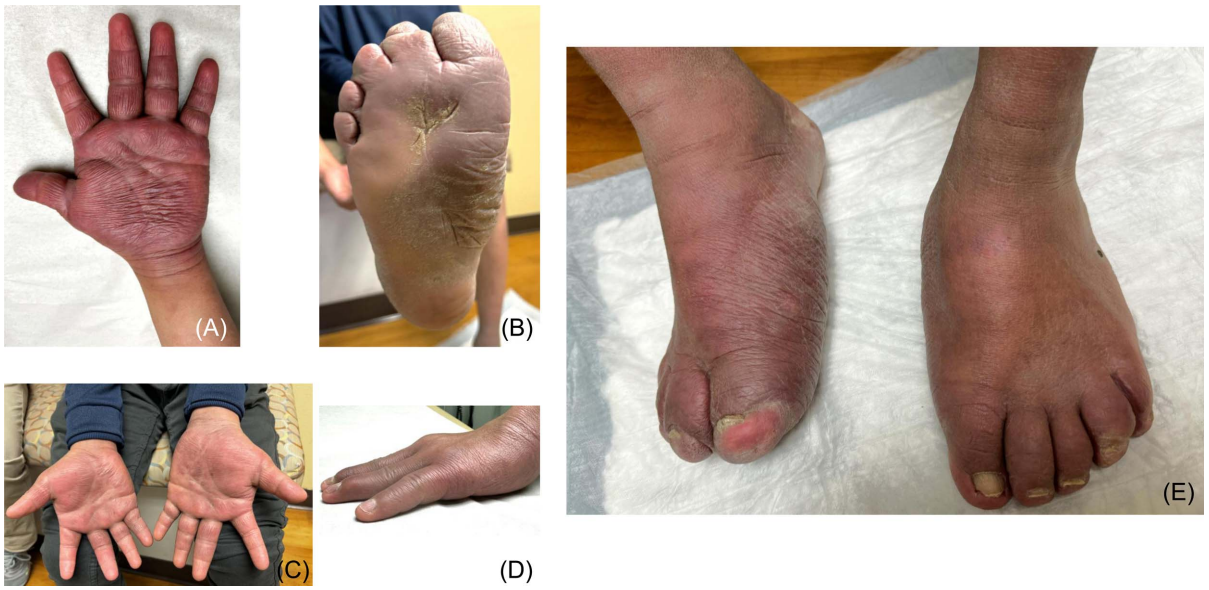

FIGURE 1.
(A) Left palm and fingers with diffuse enlargement and soft tissue thickening and a relatively normal wrist/forearm. (B) Right sole with diffuse enlargement and soft tissue thickening resulting in the appearance of pes planus. (C) Bilateral palmar involvement. (D) Lateral view of the left hand showing soft tissue thickening. (E) Feet showing sausage-like digits, dystrophic nails, pes planus, and striking soft tissue thickening and feet enlargement.

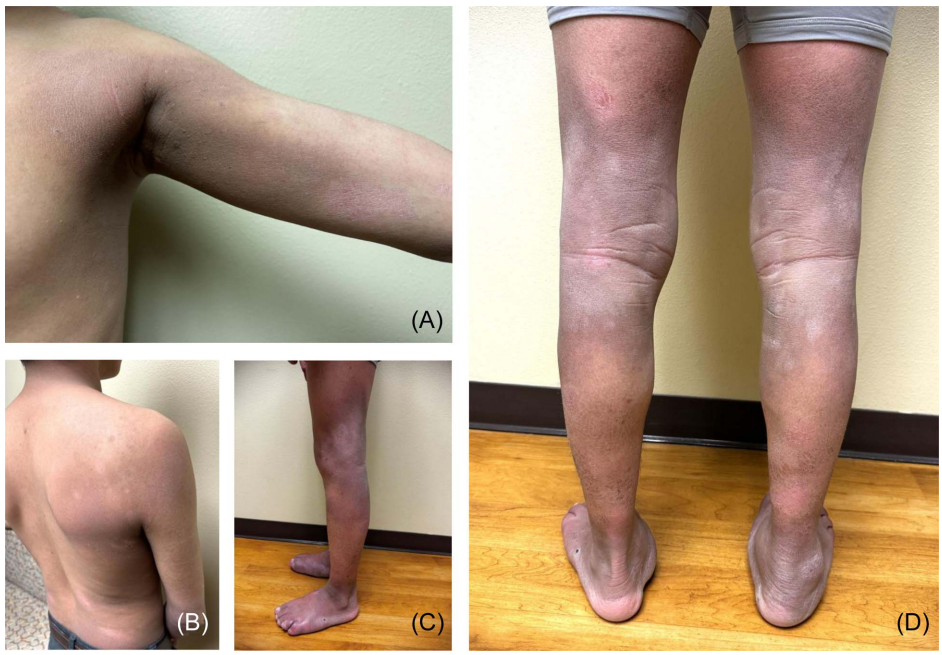

FIGURE 2.
(A) Left axilla with a hyperpigmented and lichenified plaque. (B) Right upper back and shoulder with a mildly erythematous hyperpigmented and lichenified plaque. (C) Left lateral leg showing the extent of the posterior leg rash. (D) Posterior legs with erythematous hyperpigmented and lichenified plaques expanding from the popliteal fossa.

abnormalities. As such, the above conditions were felt to be sufficiently ruled out. An internal primary care dermatology referral was made, leading to a 4-mm punch biopsy of the palm.

The biopsy revealed an atypical superficial and deep dermal CD4+ T-cell predominant infiltrate. Some spongiosis was present in the overlying epidermis with minimal intraepidermal lymphocytes. Lymphoid atypia was noted, as well. Additional immunostains showed a striking predominance of CD4+ cells. These findings raised concern for CTCL (Figure 3). However, the presence of a CD4+ T-cell infiltrate also necessitated consideration of primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (PCSM-LPD)[11] and T-cell leukemia/lymphoma due to human T-cell lymphotropic virus (HTLV)-1 infection.[12] The former typically presents as a solitary lesion, most often on the head and neck, and is less likely to disseminate.[13] Histologically, the infiltrate in PCSM-LPD often has a prominent admixture of reactive B cells and plasma cells,[14] which was not present in our case. Additionally, HTLV-1 and -2 antibodies were tested and found negative. Furthermore, tissue T-cell receptor gene rearrangement analysis confirmed clonality, which sufficiently ruled out benign dermatoses or pseudo-T-cell lymphomas.[15] These clinicopathologic findings led to the diagnosis of CTCL.

To determine the subtype, peripheral blood flow cytometry was obtained, which showed no monotypic B-cell or aberrant T-cell populations. This, along with the lack of erythroderma or lymphadenopathy, helped exclude Sézary syndrome and advanced-stage MF with extracutaneous involvement.[16,17] Additionally, computed tomography (CT) imaging of the chest and neck showed no lymphadenopathy, cardiopulmonary, or soft tissue abnormalities. Even though a positron emission tomography–CT was ultimately denied coverage by insurance, these findings supported a nonsystemic process. Overall, the clinical progression from plaques to soft tissue infiltration of the hands and feet without systemic involvement, along with the histologic, immunohistochemical, and molecular findings, ultimately supported the diagnosis of MF. Of note, even though the most prominent findings of our patient's presentation were on the hands and feet, due to the absence of a hyperkeratotic plaques or patches strictly confined to the palms and soles, MFPP was not felt to be the correct variant of MF in our case.[5]

The patient was subsequently referred to pediatric dermatology and hematology/oncology in a tertiary academic center, located a few hours away, where he was started on high-potency topical steroids. Yet his symptoms worsened with a less than 25% increase in plaque size after 2 months. A home UVB phototherapy unit was prescribed (but subsequently denied by insurance) in conjunction with oral methotrexate, managed and monitored by primary care dermatology locally.

Compounding the situation, recent executive orders on immigration have caused significant fear within the

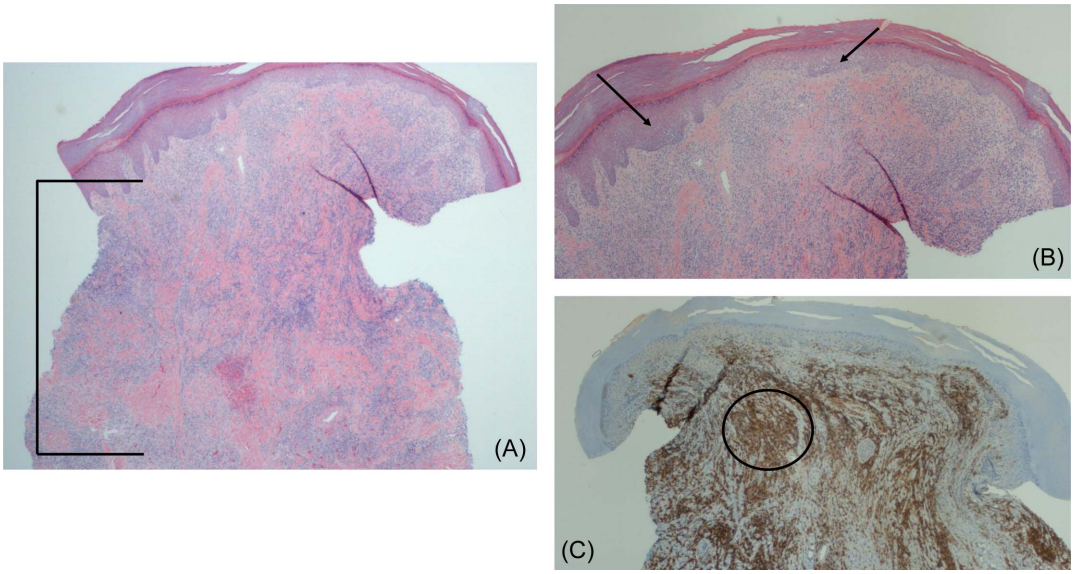

FIGURE 3.
(A) H&E stain showing an atypical superficial and deep dermal T-cell infiltrate. (B) H&E stain showing some spongiosis in the overlying epidermis with minimal intraepidermal lymphocytes. (C) CD4 T-cell immunohistochemical stain highlighting the distribution of the atypical lymphoid infiltrate. Abbreviation: H&E, hematoxylin and eosin.

patient's family and community, making it difficult for him to attend follow-up appointments with specialists. Our team, including the primary pediatrician, the primary care dermatology physician, and a case manager, are working closely with the patient's family to assist with transportation, facilitate communication with specialists, and coordinate his care.

DISCUSSION

Acral presentation of MF is exceptionally rare in children.[18] And the simultaneous involvement of all 4 digits simply has not been documented. Our case contributes to the literature in 4 key ways: (1) it expands our current understanding of MF, supporting its title of "the great imitator," (2) it highlights the need for a clearer definition of MF staging, (3) it broadens the differential diagnosis for acromegaly-like presentations, and (4) it underscores the critical role that community clinicians play in ensuring equitable care for immigrant patients, particularly amid sociopolitical challenges that hinder access to health care.

MF has been described to resemble dozens of dermatoses, including ones common in pediatric patients such as acanthosis nigricans, eczema, pityriasis lichenoides, perioral dermatitis, pityriasis alba, and vitiligo.[4] These diagnostic challenges typically occur during the patch and plaque stages of MF, which explains why MFPP is often mistaken for conditions like dyshidrotic eczema[19] or palmoplantar psoriasis.[4] In this report, we expand on MF's well-known ability to imitate other diseases by presenting a rare case of acromegaloid MF. Compared with other so-called "great imitators" such as secondary syphilis,[20] cutaneous tuberculosis,[21] and sarcoidosis,[22] our case goes to show that MF demonstrates an even greater capacity to disguise itself.

Staging posed a major diagnostic challenge, especially as a prognostic factor. Clinically, there were plaques and patches covering at least 10% of the skin surface, which classified the skin finding to at least T_{2b} (plaque-stage). However, according to current literature, histologically, plaque-stage MF typically shows epidermotropism with a superficial to mid-dermal infiltrate, whereas tumor-stage MF is characterized by dense, nodular, or diffuse infiltrates that extend deeply into the dermis and sometimes subcutis,[23] while the epidermis is often relatively devoid of tumor cells.[24] The histopathology findings of our patient's biopsy, therefore, were more indicative of a tumor-stage MF (Figure 3). This raised the question as to whether the diffuse soft tissue thickening really represented a collection of tumors in the palms and soles. According to the International Society for Cutaneous Lymphomas, a tumor is a solid or nodular lesion measuring at least 1 cm in diameter with evidence of depth and/or vertical growth.[25] Clinically, there were no distinctive tumors that might fit this definition. However, as shown in Figure 1, the enlargement of the feet was at least 1 cm in both width and thickness, which led to the patient's main concern of not finding shoes that fit. Therefore, if this acromegaloid presentation was the result of tumor infiltration, then the clinical staging would be T_3 (tumor-stage),[26] which would comport with the histological findings. To resolve this confusion with staging and classification, we propose that either the definition of "tumor" in MF staging be expanded to include an

acromegaloid presentation where the vertical or lateral growth of soft tissue exceeds 1cm, or for acromegaloid MF to be considered a separate clinical subtype of MF.

Adolescent acromegaly is extremely rare and is primarily caused by a growth hormone (GH)–producing pituitary adenoma. The typical manifestations, resulting from tumor mass effects and GH excess, include headaches, visual disturbances, menstrual irregularities (when applicable), and accelerated growth.[27] Patients often present with coarse facial features, sweating, and seborrhea.[28] Our case highlights the importance of considering CTCL as a differential diagnosis in acromegaly-like presentations that lack typical features, particularly when accompanied by a rash. Such presentations should prompt a full-thickness skin biopsy, as obtaining sufficient tissue is crucial for accurate histopathological evaluation and immunophenotyping.[29]

Our clinic is one of the largest community health centers in the Northwest, operating as a Federally Qualified Health Center (FQHC) with more than 40 locations. Research indicates that access to well-resourced FQHCs is associated with increased health care utilization among undocumented farmworkers, such as our patient's family.[30] FQHCs focus on primary care and behavioral health and often face significant challenges in accessing specialized services like dermatology.[31] These challenges are exacerbated by the significantly lower density of dermatologists in rural areas[32] and the disturbing fact that fewer than 1 in 5 dermatologists in the United States accept Medicaid.[33] It is not surprising that uninsured and Medicaid patients, like the majority of our patients, make up only a tiny fraction of dermatology clients.[34] Despite this, dermatology remains one of the most commonly requested specialty referrals in rural communities.[35] To address this gap, many community health centers turn to telemedicine for access,[36,37] which does not allow for procedural evaluation such as skin biopsy. Social stressors related to immigration status may further contribute to delays in care and decreased health care visit adherence among immigrant patients.[38] Our clinic stands out as the only FQHC and migrant health center in the country with a full-time dermatology service, a model that enabled timely evaluation and diagnosis in this case.

CONSENT

Written permission was obtained from the patient's guardian(s) to publish this case and the corresponding photos or imaging studies.

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We sincerely thank the patient and their family for their trust and willingness to share their story.

ABBREVIATIONS

CT: computed tomography
CTCL: cutaneous T-cell lymphoma
FQHC: Federally Qualified Health Center
GH: growth hormone
HTLV: human T-cell lymphotropic virus
MF: mycosis fungoides
MFPP: mycosis fungoides palmaris et plantaris
PCSM-LPD: primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder
PUVA: psoralen plus UVA
WHO: World Health Organization

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