SKIN

BRIEF ARTICLE

An Unusual Trifecta: Dermatillomania, Psoriasis, & MRSA in a Rare Case of Primary Cutaneous Gamma/Delta T-Cell Lymphoma

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ABSTRACT

Primary cutaneous gamma/delta T-cell lymphoma (PCγδTCL) is one of twelve known cutaneous T-cell lymphoma (CTCL) rare subtypes comprising of less than 1-2% of all cutaneous lymphomas. These subtypes may have either an indolent or aggressive clinical course, or may be co-existent with other dermatological, infectious, or psychiatric conditions. Based on our literature review, we were unable to find documented cases involving all three aspects of possible co-existing conditions in one patient. We present case of a 61-year-old Caucasian male diagnosed with biopsy-confirmed primary cutaneous gamma/delta T-cell lymphoma with dermatillomania, psoriasis, and MRSA.

INTRODUCTION

Primary cutaneous gamma (γ)/delta (δ) T-cell lymphoma (PCγδTCL) is one of twelve known cutaneous T-cell lymphoma (CTCL) rare subtypes comprising of less than 1-2% of all cutaneous lymphomas.[1] These subtypes, as defined by the World Health Organization (WHO), may have either an indolent or aggressive clinical course, or may be co-existent with other dermatological, infectious, or psychiatric conditions. [1,2,3,4,5,8]

PCγδTCL, more commonly affecting middle-aged to elderly men and blacks, is an aggressive lymphoma composed of clonal mature T-cells expressing T-cell receptor (TCR) γδ chains and cytotoxic molecules involving the skin and extra-nodal sites, like GI, bone, lungs, and central nervous system.[1,6] Its aggressive clinical course has an overall survival rate of 31% at two years and 11% at five years, with a median survival time of 15 months making successful treatment difficult.[1,6] A patients' medical history, along with other presenting symptoms, may convolute the clinical picture, further complicating diagnosis, and management. Thus, CTCL requires a multi-disciplinary approach.

Based on our literature review, we were unable to find documented cases involving all three aspects of possible co-existent conditions in one patient. We present the case of a 61-year-old Caucasian male diagnosed with biopsy-confirmed primary cutaneous gamma/delta T-cell lymphoma with dermatillomania, psoriasis, and MRSA.

CASE REPORT

The patient is a disheveled 61-year-old Caucasian male who presented with numerous maculopapular sores in different stages of healing on both arms, with three large, ulcerated wounds on the right upper arm, inside an annular ring (**Figure 1**). Superimposed was an area of active psoriasis along with psoriatic lesions on his arms, hands, trunk, and legs. He stated that for the past two years, he had been picking at the skin on his arms because he had a chronic sensation of "itchy bugs crawling on skin" and that he was "looking for more of 'glass' tissue that came out of it." He endorsed this being worse at night and during sleep. The repeated trauma of picking led to open sores that would itch, bleed, then inconsistency show signs of healing (**Figure 2**). However, the three areas of concern on the right upper arm had progressively gotten larger and would weep fluids over the past four months. The patient was seen by another primary care provider three months prior who treated him with mupirocin 2% topical cream daily and a prednisone 20mg taper for 16 days due to the lesions being resistant to one month of clobetasol 0.05% topical ointment. The patient had been under the recent care of a dermatologist for psoriasis but had been lost to follow up.

Past medical history included psoriasis (of seven years), insulin-requiring type 2 diabetes mellitus, anxiety, depression, cigarette smoking, alcohol abuse and illiteracy. The patient denied any history of infectious disease, including HIV/AIDS, Hepatitis B&C, tuberculosis, or cancers. The patient denied any fevers, chills, night sweats, or unexplained weight loss. Patient endorses family history of lung cancer secondary to smoking in his mother.

The wound culture of ulcerated weeping lesions resulted positive for Methicillin-Resistant *Staphylococcus aures* (MRSA). Based on sensitivities, the patient was treated with doxycycline 100mg daily for seven days (**Figure 1**). In addition, due to the unusual constellation of symptoms and history, a 5mm punch biopsy was obtained (**Figure 1**) with a differential diagnosis of pyoderma gangrenosum vs. cellulitis vs. squamous cell carcinoma. Biopsy results (**Figure 3 and 4**) showed that the lesion contained a nodular to diffuse mononuclear cell infiltrate composed of large hematolymphoid cells with intermixed small lymphocytes, histiocytes neutrophils, eosinophils, and plasma cells involving the superficial and deep dermis, with an overlying ulcerated and hyperplastic epidermis. By immunochemistry, the large cells expressed CD45, CD3 (focal), and CD56 (**Figure 5 and 6**). TCR gene rearrangement studies by polymerase chain reaction (PCR) demonstrated a clonal T-cell population. Together, these findings, along with the clinical history of non-healing wounds were most consistent with T-cell lymphoma with aggressive features. The large lesional cells labeled diffusely with CD4 and CD45 with varying intensity (**Figure 5 and 6**). CD7 and CD8 were scattered in background lymphocytes (**Figure 5 and 6**). Additional immunohistochemical stains for TCR BetaF1 and TCR$\gamma\delta$ were performed at Mayo Clinic Laboratories and were positive in large cells that also expressed CD56 and granzyme, with TCR BetaF1 positive in small background T-lymphocytes.

The patient was urgently referred to oncology for further management. PET-CT scan showed metastasis to bilateral axillary lymph nodes; however, there was no abnormal activity within the head, neck, abdomen, or pelvis. Bone marrow aspiration with biopsy and flow cytometry were both negative for

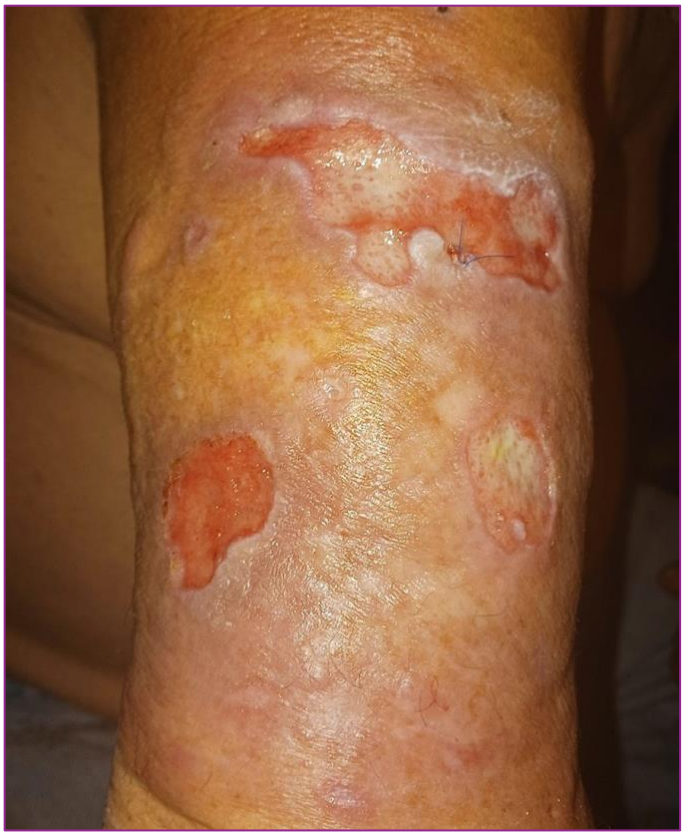

Fig. 1: Right upper shoulder with biopsy suture in place eight days after initial presentation. The patient had been on antibiotic therapy for six days for the MRSA infection.

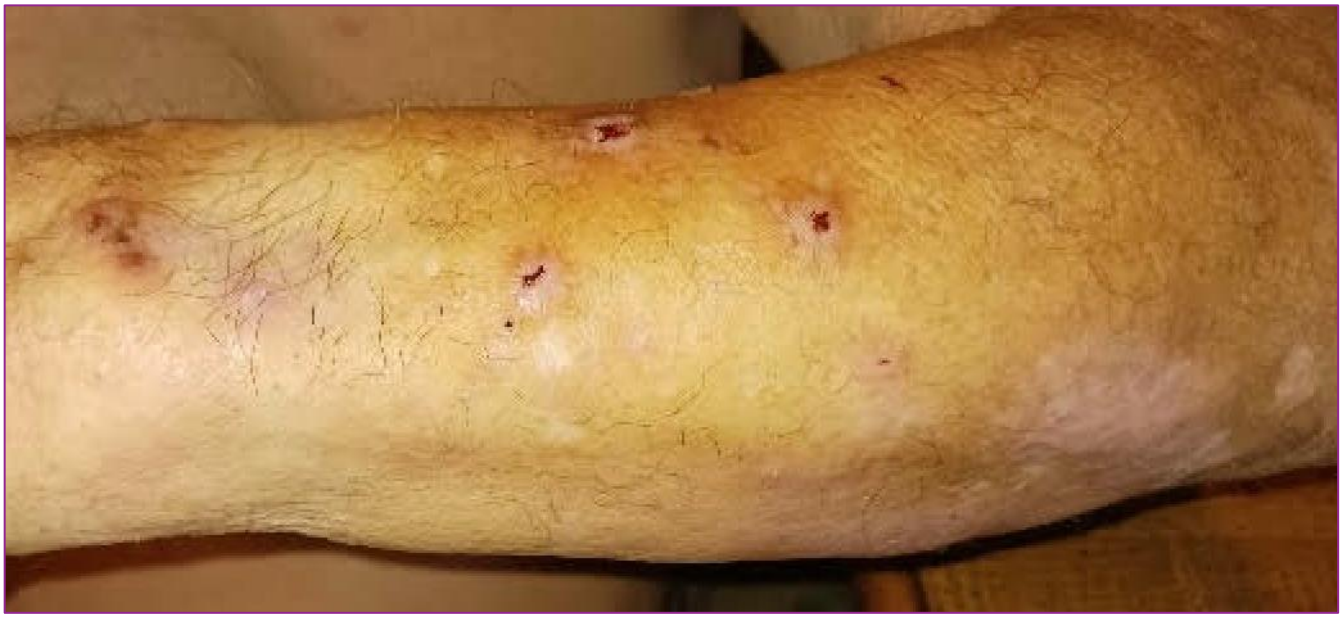

Fig. 2: Left forearm healing sores from dermatillomania with co-existing areas of active psoriasis.

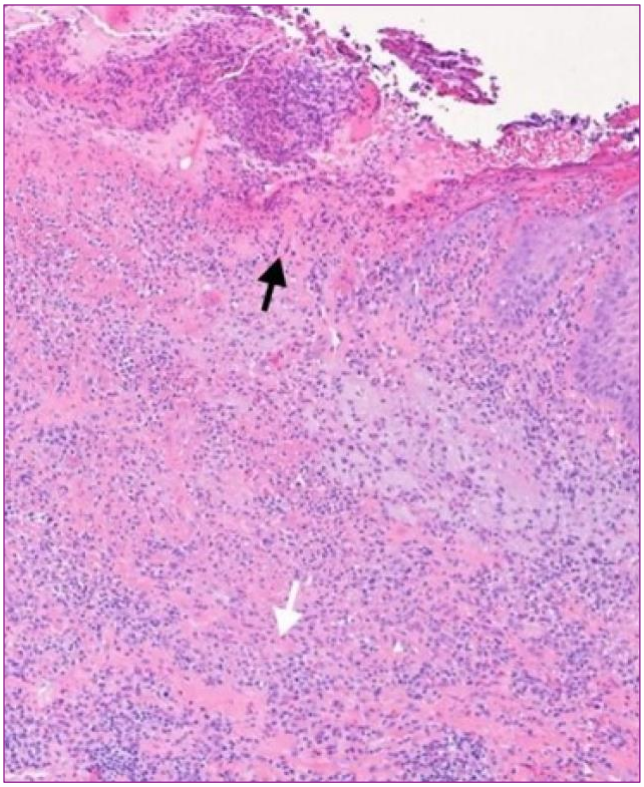

Fig. 3: Skin with ulcer (black arrow) and florid acute and chronic inflammatory infiltrate in the dermis. The lymphocyte infiltrates (white arrow) are more prominent in the deeper reticular dermis (H&E stain, x100 magnification).

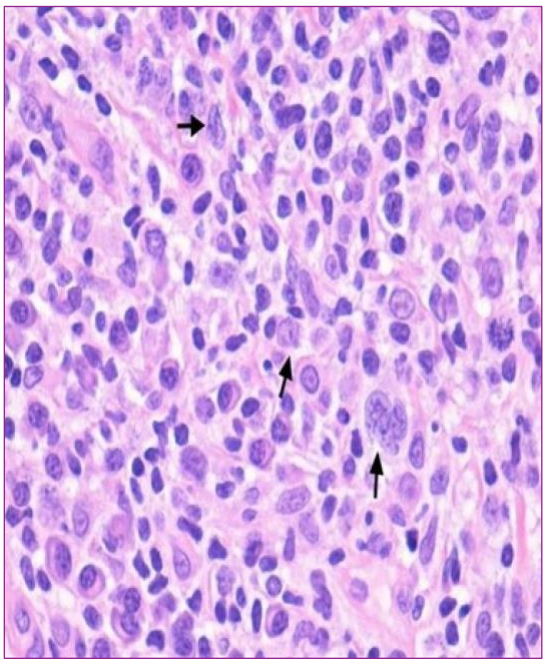

Fig. 4: Reticular dermis with malignant large lymphocytes exhibiting irregular and folded nuclei (black arrows). The background consists of benign small lymphocytes, plasma cells, and macrophages (H&E, x600 magnification).

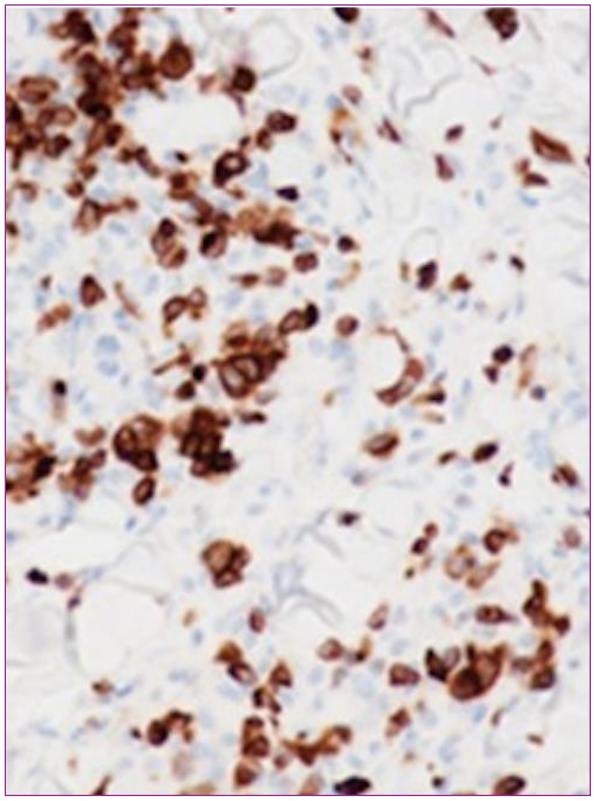

Fig. 5: Large malignant lymphocytes positive for TCR γδ immunostaining (x400 magnification).

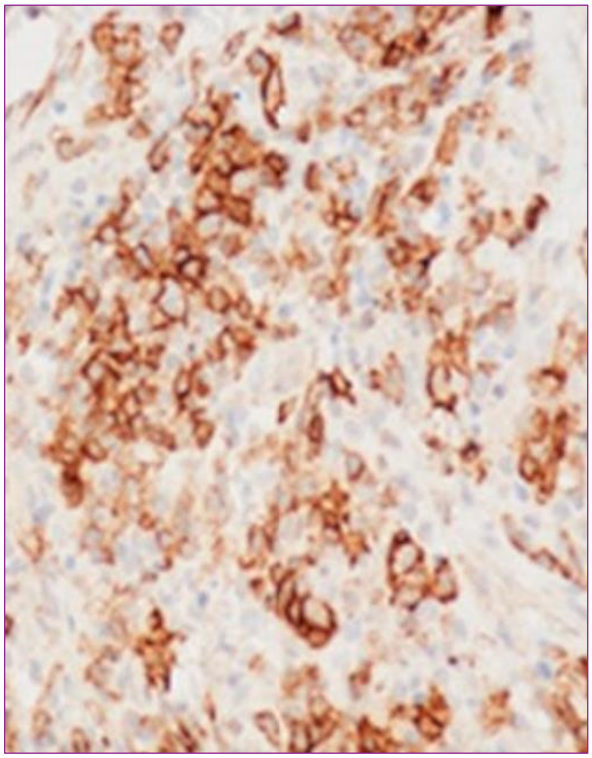

Fig. 6: Large malignant lymphocytes positive for CD56 immunostaining (x400 magnification).

lymphoma. Of note, the patient alerted the oncologist to new papular, slightly erythematous lesions on his left upper back and anterior abdominal wall—most likely new lymphomatous lesions. CHOP chemotherapy (cyclophosphamide, doxorubicin hydrochloride, vincristine, and prednisone) was recommended for treatment, with pertinent side effects discussed.

DISCUSSION

Primary cutaneous gamma/delta cutaneous T-cell lymphoma (PC*γ*δTCL) is a rare and highly aggressive subtype of CTCL with very poor prognosis.[1] In fact, in 2009, only 40 cases of PC*γ*δTCL had been documented worldwide.[7] Affected patients commonly present with multiple skin lesions, characterized by large and deep plaques, nodules, or tumors accompanied by pruritus and superimposed erosions, ulcerations, and/or infections on the upper and lower limbs or trunk.[1] PC*γ*δTCL can be distinguished from other lymphomas due to the absence of B symptoms, including fevers, night sweats, and weight loss—as seen in our patient—and uninvolved lymph nodes and bone marrow.[1]

Severe pruritus followed by scratching commonly leads to breaks in the skin barrier and results in abnormal T-cells and increased susceptibility to *S. aureus* infections.[1] *S. aureus* plays an important role in disease progression including erythroderma, exacerbation of pruritus, and increased morbidity, especially in those infected with MRSA.[4,8] It is thought that inflammation secondary to staphylococcal skin infections worsens CTCL flares because *S. aures* is found at increased rates, in those with compromised skin and immunodeficiency, like CTCL at 76%, when compared to immunocompetent hosts.[4,6,8]

It is thought that individuals with psoriasis are at an increased risk of developing CTCL.[2] However, the increased risk of lymphoma in these patients has been questioned because CTCL in its early stages may be misdiagnosed as psoriasis.[2] CTCL and psoriasis share the features of abnormal activation of T-cells and lack of circulating lymphocytes.[8] Clinicians should be aware of this possible correlation when managing patients, especially those who develop skin lesions atypical for psoriasis or those who's psoriatic lesions are refractory to treatment using immunochemistry and/or molecular biology techniques.[2,9]

Successful treatment of CTCL is difficult despite multiple implemented interventions. PC*γ*δTCL has high resistance to polychemotherapy and radiotherapy, leading to median survival of 15 months from the time of diagnosis.[1,7] When started early in disease progression, allogeneic stem cell transplant can result in long-term remissions in some patients. [6] Other therapies include CHOP, EPOCH (etoposide + CHOP), ICE (ifosfamide, carboplatin, and etoposide), and Hyper-CVAD (hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone.[10] At least five previous cases had a positive clinical response to brentuximab vedotin after several months of treatment.[11] It is important to note that studies/cases that utilize these drugs are from case series with small number of patients, which limit the ability to draw solid conclusions.[1,10]

Due to its rapid sequalae, clinicians should prioritize a patient's quality of life (QoL) and its psychosocial burden during management. Studies show that patients' higher psychological resilience, younger age, and high education level correlate positively with patients' ability to process, cope with their new normal because they show a greater

adherence to treatment.[5,12] With our patient of low socioeconomic background and illiteracy to both reading and writing, along with anxiety and depression, it will be even more imperative to utilize the multi-disciplinary approach, utilizing social services, psychiatry, and counseling services, in conjunction to oncology to maximize cognitive resources for appropriate coping and also mitigate maladaptive outcomes that would negatively impact the patient's adherence to treatment and overall health outcomes.[5,12]

Pruritus is a common symptom experienced by those with CTCL independent of disease stage.[13] It is thought that this malignancy-associated pruritus is the result of the neoplasm's local effect on tissue via cytokine interleukin (IL)-31 of the IL-6 family, a histamine-independent mediator, primarily produced by CD4 helper T-cells or the systemic reaction to malignancy[3,14] which can range from a negligible irritation to a tormenting sensation that greatly impacts their lives.[13] For example, decreased mood and impaired sleep.[13] In addition to the psycho-dermatological aspect of disease burden, pruritus has also been associated with a decreased QoL.[13] As described in the case description, the patient experienced the sensation of "itchy bugs crawling on skin" leading to repeated skin picking and trauma. It is unclear what the patient was attempting to describe when stating he was "looking for more of 'glass' tissue that came out of the wound. This could possibly be the result of the patient's anxiety or another undiagnosed psychiatric condition.

Studies have shown that there is a strong negative correlation between those with CTCL who experience pruritus and their QOL.[13] Therefore, management of this condition should also include optimal control of pruritus. High potency topical corticosteroids in early state CTCL are often used, but with disease progression, patients commonly report an ill-defined, severe, and diffuse pruritis that feels more like a "burning pain," similar to neuropathic pain.[3] Gabapentin 300-2400mg daily and mirtazapine 7.5-15mg daily, along with a prednisone taper starting at 40mg over three weeks, have been reported to be efficacious in the treatment of itch for CTCL.[14]

CONCLUSION

This unique and unexpected case of PCγδTCL further demonstrates the difficulty and complexity of making an early and accurate diagnosis of cutaneous lymphomas which helps maximize patient outcomes. Due to the rarity of these disorders, and the additional burden of possible co-existing conditions, more data is needed to further guide therapeutic approaches.

Conflict of Interest Disclosures: None

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