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Erythrodermic mycosis fungoides with large cell transformation: An unusual and complicated case

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Abstract

Mycosis fungoides is the most common cutaneous T-cell lymphoma. It presents a diagnostic challenge due to resemblance with many other dermatologic conditions. The disease typically follows a progression from patches to plaques to skin-based tumors with potential for visceral involvement. Diagnosis is made by clinical presentation and histology. When early diagnosis is made, there is an estimated 88% five-year survival. This report details a 60-year-old Black man diagnosed with stage IIIA mycosis fungoides with a severe degree of cutaneous involvement. This case is unique due to the aggressive large cell transformation and rapid progression to death within 18 months of diagnosis. We highlight the challenge of diagnosing, treating, and monitoring the therapeutic response of mycosis fungoides. Finally, this case calls for a multi-disciplinary approach to treatment and to include mycosis fungoides on the differential diagnosis for patients presenting with a variety of vague, recurrent cutaneous symptoms, especially with patchy dyspigmentation or plaques.

Keywords

Mycosis fungoides, large cell transformation, wound infection, pruritus, COVID-19

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Introduction

Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma (CTCL), accounting for 70% of CTCL diagnoses.[1] MF is rare with an incidence of 0.29 per 100,000 persons and has a predominance for patients that are male and/or Black. The disease typically follows a progression from patches to plaques to skin-based tumors with potential for visceral involvement.[2] Diagnosis is made through a combination of clinical presentation and histology. The initial patches vary in size and shape, can be erythematous or hypopigmented, have a scaly surface, and may present on sun-protected areas. MF diagnosis is confirmed by histology showing infiltrates of small-to-medium cells with hyperchromatic, characteristically cerebriform nuclei. Flow cytometry reveals immunopositivity for CD3 and CD4.[3]

The pathogenesis of MF is unknown but is believed to be linked to T-cell overstimulation. Although viruses are thought to play a role in the pathogenesis of adult T-cell lymphoma, no causative mechanism has been established between MF with positive serologies for human T-cell lymphotropic virus (HTLV), Epstein–Barr virus, or cytomegalovirus.[4–6] The malignant T-cells of MF show a tropism for the skin as mediated by interactions between surface T-cell CCR4 receptors and dermal chemokines including CCL17 and CCL22.[6] The degree of skin involvement determines the T-stage according to tumor node metastasis (TNM) classification.[7]

We present a unique case report of MF on a patient that initially presented with eczema-like symptoms, progressing

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to severe ulcerations, underwent large cell transformation and care complicated by COVID-19 hospitalizations. Reporting for this article is in line with the CARE Case Report Guidelines.[8]

Case presentation

A 60-year-old male with past medical history significant for vitiligo and anemia presented to the emergency department (ED) in August 2019 with chief complaint of diffuse itchy skin over his entire body for several weeks. No exacerbating or remitting factors were noted. Three weeks prior, the patient was diagnosed by his primary care physician (PCP) with dermatitis from a punch biopsy treated with topical nystatin. The patient reported occupational exposures working at a metal refinery and at a shipping dock. He was an active pack-per-day smoker with a 35-year history, drank alcohol daily, and denied illicit drug use. He was sexually active with multiple female partners, reported no significant family history nor travel outside of the United States.

Physical exam revealed dry circular rashes with widespread inguinal, axillary, and supraclavicular adenopathy. Laboratory analysis with complete blood count, comprehensive metabolic panel, lactate dehydrogenase, and angiotensin-converting enzyme were within normal limits. Human immunodeficiency virus serology was negative. He was discharged with diagnosis of nummular eczema treated with topical hydrocortisone 2.5% applied twice daily, cetirizine 10 mg tablet once daily, naproxen 500 mg twice daily, and a 40 mg oral prednisone taper.

A month later, in September 2019, he followed-up with the PCP due to unremitting itching. Edematous nasal mucosal, posterior oropharyngeal erythema, and a maculopapular erythematous rash were found on physical exam. He was treated with topical triamcinolone 0.5% ointment twice daily and hydroxyzine 10 mg three times daily.

In January 2020, he was referred to Dermatology for persistent intense pruritus. Physical exam revealed lesions on his face, chest, and abdomen. He, otherwise, felt well and denied constitutional symptoms. A documented differential diagnosis included sarcoidosis, lichen planus, disseminated lupus erythematosus, lymphoma, and syphilis. Punch biopsies were performed on lesions located on the left upper chest and abdomen. Results showed morphologic, immunophenotypic, and molecular findings from both biopsies consistent with CTCL; immunophenotype CD3+, CD4+, CD8+, CD4:CD8 ratio > 2:1, significant loss of CD7 lymphocyte staining, CD20 highlighted rare-scattered B lymphocytes, CD30+ was present in less than 5% of observed cells, and Treponema pallidum stain was negative. T-cell gene rearrangement studies were positive for a monoclonal T-cell population. Histologically, there was atypical lymphoid epidermal infiltrate with highly irregular nuclear contour, splitting at the dermal/epidermal junction consistent with blister formation, and inflammatory dermal infiltrate with small lymphocytes, histiocytes, and eosinophils. With these results, the patient was referred to Dermatology, Hematology, and Oncology.

In February 2020, a computed tomography (CT)/positron emission tomography scan was done, which revealed moderately avid and enlarged bilateral axillary, inguinal, and supraclavicular lymph nodes. Pathology from an ultrasound-guided left axillary lymph node biopsy demonstrated CTCL. Tumor staging was IVA2 with T4N3M0B0 classification with more than 80% cutaneous involvement, clinically abnormal peripheral lymph nodes with pathology positive for CTCL. CD25 staining was conducted and found to be negative. Serology for HTLV-1 was not obtained as the patient was deemed low risk for exposure based on travel history. Treatment was initiated with doxepin 25 mg capsule and warfarin 1 mg tablet once daily. The patient requested a second opinion and was evaluated by Cleveland Clinic Oncology in April 2020, which confirmed the diagnosis. Clobetasol 0.05% topical cream twice daily, desonide twice daily, oral bexarotene 200 mg/m^2, and gabapentin 300 mg capsule once daily were added. In December 2020, the patient presented to the ED complaining of bilateral foot pain and swelling. Workup with bilateral lower extremity duplex was negative and the patient was discharged.

In January 2021, he returned to the ED with extreme pain and several open skin wounds draining yellow–green fluids (Figure 1). Physical exam revealed a large eschar draining foul-smelling fluid on the chest and multiple excoriating wounds covering more than 70% of the body. He was admitted for wound care and broad-spectrum antibiotics. CT chest/abdomen/pelvis showed significant axillary adenopathy, enlarged bilateral inguinal and external iliac chain lymph nodes, and multiple subcutaneous lesions along the ventral abdominal wall. Staging at this point was T4N3M0B0. Skin cultures from the right chest grew methicillin-resistant Staphylococcus aureus (MRSA) and Diphtheroid. On hospital day 2, he was taken to the operating room for left inguinal lymph node excision, left anterior abdominal wall biopsy, and debridement of a chest wall eschar. Pathology from the inguinal lymph node and biopsy showed MF with large cell transformation. Bexarotene therapy was discontinued given worsening skin lesions and romidepsin 14 mg/m^2 on days 1, 8, and 15 of a 28-day treatment cycle was initiated. Due to COVID-related facility utilization, daily requests for transfer to a dedicated burn intensive care unit (ICU) were denied and eventual discharge to a skilled nursing facility (SNF) was delayed by 6 days to admission day 14.

In February 2021, the patient presented for a Wound Care Clinic follow-up visit with diffuse large lesions draining purulent foul-smelling discharge (Figure 2). Due to the severity of the wounds, the patient was transferred to the ED. He was subsequently admitted for excruciating pain and infected skin lesions covering more than 80% of his body. On admission, the care-navigation team revealed the patient was

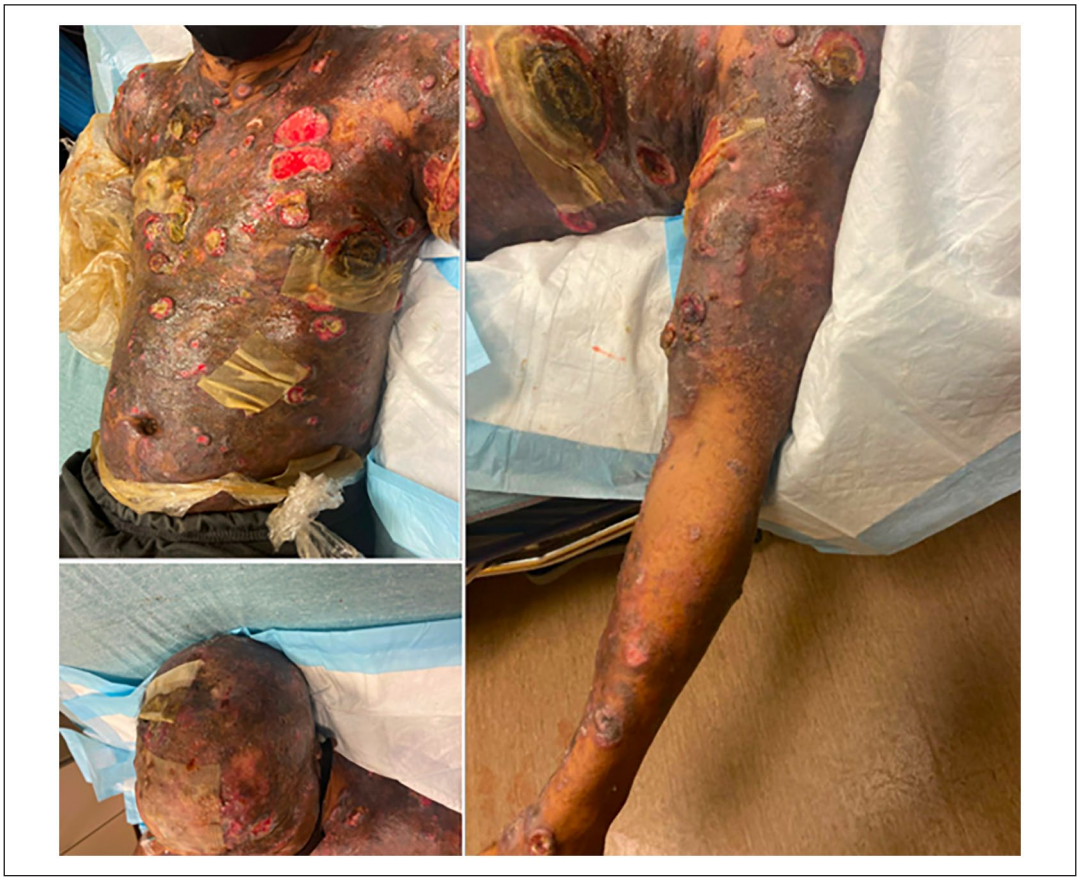

Figure 1. Emergency department photos from initial admission showing diffuse wounds with necrosis.

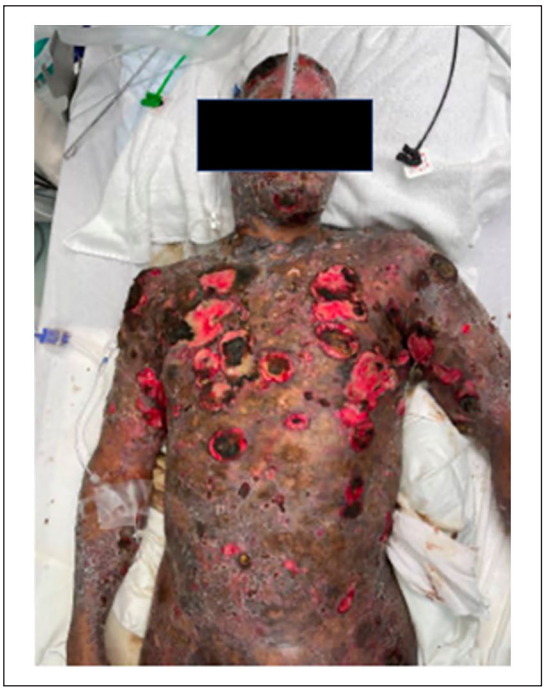

Figure 2. Image from the patient's second hospital admission just prior to wound debridement.

supposed to be discharged to a long-term acute care (LTAC) facility, not to an SNF. Despite recommendation for transfer to a burn intensive care unit (ICU), five facilities denied the request. Aggressive pain management and broad-spectrum antibiotic therapy were initiated and romidepsin was held due to the complex wound infections. On admission day-2, extensive excisional debridement of necrotic tissue located on the left buttock, back, chest, abdomen, and bilateral upper extremities were performed (Figure 2). Wound cultures returned positive for MRSA and blood cultures revealed group B Streptococcus bacteremia. Staging at this point was T4N3M0B1.

Post-operatively, the patient remained on mechanical ventilation and was transferred to the surgical ICU. His condition continued to deteriorate and on admission day-4, he became critically hypotensive with decreased urine output and leukocytosis. Repeat blood cultures returned positive for group G streptococcus and MRSA bacteremia. On admission day-6, the patient failed a spontaneous breathing trial. On admission day-10, family changed the patient's code status to do not resuscitate with comfort care only and the patient was extubated. Four days later, on admission day-14, the patient expired. Timeline of events for this patient's case are shown in Figure 3.

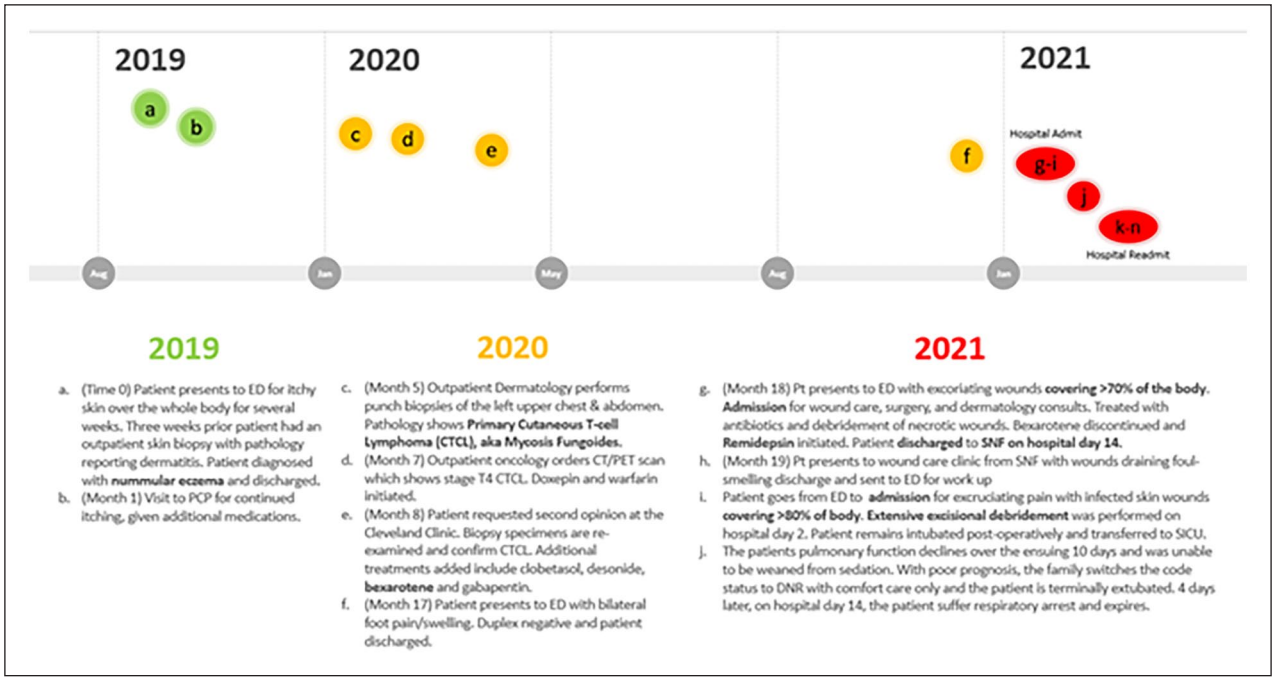

Figure 3. Timeline of events.

Discussion

Prompt diagnosis of MF is difficult due to similarity to other dermatologic conditions. Early on, MF presents like contact dermatitis, eczema, psoriasis, lichen, and cutaneous drug reactions.[3] In our case, the patient was initially diagnosed with dermatitis followed by nummular eczema and finally MF.

In its early stages, MF is indolent, with Stage IA patients having 98% 5-year survival rates.[1] However, the 5-year survival in advanced MF with secondary bacterial infection is around 20%.[9] The most common cause of death in MF patients is sepsis, often from Staphylococcus aureus introduced through breaks in the skin.[10] The patient in this case had numerous skin and systemic infections. MF may undergo large cell transformation, which has a poor prognosis with average survival of 18–36 months.[11] Our patient suffered such transformation and expired <1.5 years from initial diagnosis. Tumor stage is correlated with the likelihood of transformation, with <15% risk in Stage I–IIa and ~30% in Stage IIb–IV.[12]

The goal of therapeutic management of MF is remission. Early MF (Stage I–IIA) is treated primarily with topical therapy including corticosteroids, nitrogen mustard, phototherapy, antipruritics, and prophylactic antibiotics for open skin wounds.[13,14] Systemic therapies with antineoplastics and biologics are implemented for Stage IIB–IV MF.[14] In our patient, bexarotene was initially prescribed but discontinued due to lack of wound improvement, followed by romidepsin.

Several components of this patient's care added to the complexity of this case. This patient's complicated wounds required more intensive care than what SNF could provide. Both the discharge to the SNF, instead of an LTAC, and the inability to transfer him to a burn ICU were limited by facility crowding from the COVID-19. This highlights the importance of a multi-disciplinary approach to CTCL management, the necessity of early referral to specialized centers, and the disruption to oncologic patient care in the era of the pandemic.

Conclusion

Three key takeaways from this case should be noted. First, MF should be included on the differential for patients with chronic, atypical, widespread skin lesions. Second, management of MF requires multi-disciplinary approach with early referral to specialized centers to reduce morbidity. Finally, the COVID-19 pandemic caused significant disruption to the appropriate care of many oncologic patients.

Author contributions

C.V.L. was involved in the investigation, coordination, writing (original and final draft), reviewing, and editing. W.H. contributed to investigation, writing (original draft), reviewing, and editing. L.D.G. contributed to writing (original draft), reviewing, and editing. S.V. reviewing and editing. M.T.A. was involved in reviewing and editing. A.G. contributed to reviewing and editing of the article.

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Ethical approval

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Informed consent

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