Nail Alterations in Cutaneous T-Cell Lymphoma: A Case Series and Review of Nail Manifestations

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Key Words

Cutaneous T-cell lymphoma · Mycosis fungoides · Sézary syndrome · Nail manifestations

Abstract

Background: Cutaneous T-cell lymphoma (CTCL) encompasses a broad range of lymphoproliferative diseases affecting the skin and can be clinically misleading due to its variable presentation. Nail alterations commonly appear in advanced-stage mycosis fungoides and true Sézary syndrome; however, they may be present in any stage of the disease. Although proper recognition of nail involvement in CTCL has both clinical and therapeutic value, specific nail findings have been infrequently described in the current literature. **Observations:** We describe 4 patients with CTCL who presented with clinically significant nail alterations. The most common findings were nail discoloration, thickening, crumbling, onycholysis, and onychomadesis. Other notable findings included splinter hemorrhages, subungual hyperkeratosis, and anonychia. **Conclusions and Message:** The

described cases illustrate many of the documented nail findings associated with CTCL and emphasize the variable nature of nail manifestations. The presence of specific nail alterations should increase the clinical suspicion of CTCL – especially in patients with concomitant systemic and/or cutaneous manifestations – and early biopsy specimens should be taken for diagnosis. Nail alterations should also be accurately described and monitored in all patients with biopsy-confirmed CTCL to help identify treatment response and detect disease recurrence.

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Introduction

Cutaneous T-cell lymphoma (CTCL) encompasses a broad range of lymphoproliferative diseases affecting the skin and can be clinically misleading due to its variable appearance. Mycosis fungoides (MF) is the most common variant of CTCL and is characterized by a malignant T-cell population that is confined to the skin. Sézary syn-

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Fig. 1. Yellow discoloration, distal splinter hemorrhages, onycholysis, and proximal onychomadesis on the right thumb nail.

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Fig. 3. Severe thickening, crumbling, and yellow-brown discoloration of all nails.

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Fig. 2. Severe thickening, crumbling, and yellow-brown discoloration of all nails with onycholysis, onychomadesis, and subungual hyperkeratosis.

drome (SS) is the leukemic variant of CTCL and is defined by the presence of erythroderma, generalized lymphadenopathy, and circulating Sézary cells in the peripheral blood ($>1,000/\mu\text{l}$) according to the World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC) classification of cutaneous lymphomas [1]. The clinical presentation of CTCL typically includes a combination of systemic, cutaneous, and nail manifestations with a marked variability. Nail alterations generally occur later in the disease and affect multiple digits. However, nail involvement is often unpredictable and infrequently described in the current literature.

Case Reports

We describe 4 patients with CTCL who presented with clinically significant nail alterations. All patients described have given their informed consent, and the study has been approved by the Institutional Review Board of the University of Miami Leonard M. Miller School of Medicine.

Case 1

A 62-year-old Caucasian male presented with a 3-year history of CTCL. His treatment regimen included monthly photopheresis, apremilast, and topical emollients for the past 2 years. On physical examination, diffuse erythroderma and xerosis were observed bilaterally. Keratoderma, xerosis, fissuring, and mild swelling were appreciated on bilateral palmar surfaces. Nail alterations were observed in 5 of 20 nails. Nail discoloration and thickening were appreciated in all 5 of the affected nails. Onycholysis and onychomadesis were observed in 3 of the 5 affected nails. Other notable findings included splinter hemorrhages, severe crumbling, anonychia, and increased lateral curvature of the affected nails (fig. 1).

Case 2

A 71-year-old Hispanic female presented with a 2-year history of erythrodermic MF and concomitant alopecia universalis. Her treatment regimen included acitretin 25 mg daily with photopheresis. On physical examination, all 20 nails showed severe thickening, crumbling, and yellow-brown discoloration. Onycholysis and onychomadesis with partial nail shedding and subungual hyperkeratosis were also appreciated in all 20 nails (fig. 2).

Case 3

A 65-year-old Hispanic female presented with erythrodermic MF/Sézary overlap syndrome and concomitant alopecia universalis. Her treatment regimen for CTCL included extracorporeal photopheresis and methotrexate. On physical examination, all 20 nails showed severe thickening, crumbling, and yellow-brown discoloration (fig. 3).

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Fig. 4. Severe thickening, crumbling, subungual hyperkeratosis, and yellow-brown discoloration.

Case 4

A 65-year-old, darker-pigmented male presented with a 2-year history of MF. His treatment regimen included photopheresis and oral bexarotene. On physical examination, erythroderma, palmoplantar keratoderma, and diffuse lymphadenopathy were evident. Severe nail thickening, crumbling, subungual hyperkeratosis, and yellow-brown discoloration were observed in all 20 nails (fig. 4).

Discussion

Nail manifestations of CTCL commonly appear in advanced-stage MF and true SS but may be present in any stage of the disease. Although nail manifestations are not diagnostic, recognition of nail involvement is an important component of disease management that has both clinical and therapeutic value. Clinically, the presence of nail alterations may be helpful in evaluating the response to systemic therapy and identifying disease recurrence. Nail alterations refractory to systemic therapy may also alter the therapeutic management and/or require additional localized treatment regimens.

Previously reported cases of biopsy-confirmed MF have included nail discoloration [2–4], thickening [2–5], onycholysis [3, 5, 6], onychomadesis [2], subungual hyperkeratosis [5], pterygia formation [6, 7], and other, less specific changes. Plaque and tumor stage MF has also been associated with the ‘yellow nail syndrome’, which is characterized by specific nail alterations and may present with chronic respiratory disorders and lymphatic dysplasia [2].

Onycholysis and Onychomadesis

Onycholysis has been reported in several cases of MF [2, 3, 5, 6] and is caused by detachment of the nail from the nail bed at the distal and/or lateral attachment sites. It generally extends proximally until it reaches the nail matrix and can progress to onychomadesis. Onychomadesis occurs when severe onycholysis causes separation of the nail plate from the nail matrix [8]. Onychomadesis was first documented in a patient with biopsy-confirmed multi-plaque stage MF who presented with a modified version of the yellow nail syndrome. Nail findings included a slow nail growth, discoloration, thickening, overcurvature, and shedding of all 20 nails without exaggerated lateral curvature. Symmetrical proximal onycholysis consistent with onychomadesis was also observed, an unusual finding in nonerythrodermic MF. Treatment with fractionated electron beam radiation was effective in achieving complete remission of all cutaneous findings [3].

Subungual Hyperkeratosis

Subungual hyperkeratosis is characterized by thickening of the nail bed or hyponychium [8]. Harland et al. [5] first reported the presence of subungual hyperkeratosis in a MF patient who initially presented with paronychia and onycholysis of the right thumb. The nail involvement gradually progressed to involve all 10 nails with marked paronychia, trachyonychia, complete onycholysis, and subungual hyperkeratosis. A biopsy of the nail matrix confirmed the presence of ungual MF, and systemic chemotherapy with gemtubicine resulted in complete remission.

Pterygium Formation

More recently, the presence of pterygia has been reported in addition to previously described nail changes. Pterygia appear as a progressive, wing-shaped scar in the nail area and cause irreversible damage [8]. Mazzurco et al. [6] described a patient with a 10-year history of nail lichen planus who presented with erythematous, fissuring, scaling plaques in the bilateral thumb-nail folds and stable onycholysis with pterygia formation in the remaining 8 nails. Biopsies of the nail bed and matrix confirmed the presence of ungual MF. Both thumb lesions were resistant to psoralen and ultraviolet-A light (PUVA) therapy, topical retinoids (tazarotene and bexarotene), and class I topical steroids but responded to orthovoltage spot radiation, achieving complete remission. Another report described a patient who presented with anonychia and pterygia in all 20 nails and associated palmoplantar in-

volvement. Epidermal biopsies confirmed a diagnosis of folliculotropic MF, and PUVA therapy resulted in a marked improvement [7].

Other Findings

Less specific nail findings, including trachyonychia [4, 5] and paronychia [5], have also been identified in multiple studies. These findings generally appear with more specific nail alterations and/or concomitant systemic manifestations. However, Toritsugi et al. [4] described a patient with vesiculopustular palmoplantar MF who presented with rough, yellow, and thickened nail plates in the absence of systemic findings. Single-digit involvement has also been described in a patient with tumor stage MF. Nail alterations on physical examination included onychodystrophy, nail plate thinning, and partial obliteration of the proximal and distal nail folds. T-cell immunoprofiling revealed a marked elevation of the CD4:CD8 ratio (>10:1), and localized radiation resulted in anonychia and complete resolution of the tumor [9].

Sézary Syndrome

Nail involvement is a common clinical feature of SS that may include yellow discoloration, nail plate thickening [10–12], subungual hyperkeratosis [10, 13–15], onychodystrophy [15], splinter hemorrhages [14], onychomadesis [12, 15], trachyonychia [15], and/or indentations of the nail [14]. Tomsick [13] first described the presence of subungual hyperkeratosis in a patient with multiple MF plaques and circulating Sézary cells. Dalziel et al. [10] similarly described marked subungual hyperkeratosis with roughened nail plates and loss of normal sheen in an elderly woman with true erythrodermic SS. A review of 5 SS cases found that all 5 patients presented with splinter hemorrhages in at least 5 nails. Yellow-brown discoloration was observed in 4 of the 5 cases, subungual hyperkeratosis and onycholysis in 3, nail plate thickening in 2, and large, irregular indentations were observed in 1 patient [14]. Tosti et al. [11] also described nondiagnostic nail plate thickening and discoloration in a patient with nail biopsy-confirmed SS. More recently, Parmentier et al. [12] described a patient who presented with isolated onychomadesis in the absence of nail discoloration, growth arrest, or subungual hyperkeratosis in 9 of 20 nails. Finally, a retrospective review of 15 SS patients with nail involvement found yellow discoloration to be the most common nail finding at presentation (7/15), followed by nail plate thickening (6/15), onychodystrophy (6/10), subungual hyperkera-

tosis (4/15), onychomadesis (3/15), and trachyonychia (2/15) [15].

In conclusion, identification of nail alterations associated with CTCL is often a challenge due to the variability of its clinical presentation. These cases illustrate many of the previously reported nail findings in patients with CTCL and emphasize the variable nature of associated nail manifestations. The presence of nail discoloration, thickening, crumbling, onycholysis, onychomadesis, onychodystrophy, subungual hyperkeratosis, splinter hemorrhages, and pterygia formation should raise suspicion of CTCL – especially in patients with additional systemic and/or cutaneous findings – and early biopsy specimens should be taken for diagnosis. Nail alterations should also be accurately described and monitored in all patients with biopsy-confirmed CTCL as they may provide useful information regarding treatment response and disease recurrence. Although specific nail involvement in patients with CTCL is uncommonly reported and often difficult to identify, it should be properly recognized and considered in all patients.

Statement of Ethics

All patients described have given their informed consent, and the study has been approved by the Institutional Review Board of the University of Miami Leonard M. Miller School of Medicine.

Disclosure Statement

The authors do not have any personal conflicts of interest.

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