Case Report

Non-Dermatophyte Onychomycosis Caused by *Aspergillus* in a Patient with Systemic Lupus Erythematosus: A Case Report

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Abstract

Onychomycosis is a fungal infection of nails, occasionally found on fingernails. Non-dermatophytes molds (NMDs), such as *Aspergillus spp.*, are increasingly reported, particularly in immunocompromised patients. We report a case of a 19-year-old female with systemic lupus erythematosus (SLE), treated with immunosuppressive drugs, presenting with proximal subungual onychomycosis. Fungal cultures confirmed *Aspergillus flavus*. The patient achieved complete clinical and mycological cure after three months of pulsed oral itraconazole therapy. This case emphasizes the need for proper mycological diagnosis in immunocompromised patients presenting with nail abnormalities.

Keywords: non-dermatophyte onychomycosis, *Aspergillus* onychomycosis, systemic lupus erythematosus, itraconazole.

How to Cite this: Sintia DD, Umborowati MA, Suyoso S, Ervianti E, Astari L, Mapamasing H, et al. Non-Dermatophyte Onychomycosis Caused by Aspergillus in a Patient with Systemic Lupus Erythematosus: A Case Report. J Pak Assoc Dermatol. 2025;35(3):264-267.

Received: 30-08-2024 **Revision:** 28-06-2025 **Accepted:** 31-07-2025

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Introduction

Onychomycosis is a fungal nail infection that accounts for 50–60% of nail diseases globally, with a prevalence of approximately 10%.[1] It is less commonly found on fingernails. In Indonesia, the incidence ranges from 10.8% to 15%.[2] Clinical features include nail discoloration, thickening, and dystrophy. Mixed infections involving dermatophytes, non-dermatophytes, and yeasts are increasingly reported, particularly in warm and humid climates.[1,2] Onychomycosis can be challenging to treat and is associated with high recurrence rates and treatment failure.

Non-dermatophytes Molds (NMDs) are responsible for 3-25% of all onychomycosis cases, with *Aspergillus spp.* occurs in 0,5-3% cases.[3] Over 300 Aspergillus species have been identified worldwide, including *Aspergillus flavus, Aspergillus fumigatus, Aspergillus nidulans,* and *Aspergillus niger*. It is commonly inhabiting soil, decaying vegetation, water, and animals including pets.[4-5]

Case Report

A 19-year-old female with systemic lupus erythematosus (SLE) presented with a two-month history of nail discoloration and brittleness on the third and fourth fingers of her left hand. She reported progressive thickening and fragility of the nails without associated pruritus or trauma. Initial self-management by trimming the nails did not improve her condition.

During a prior hospitalization for SLE, she was referred to the dermatology department for evaluation regarding damaged nails. Physical examination showed subungual hyperkeratosis, proximal onycholysis, destruction of the proximal nail plate and dyscromia on the affected nails (Figure 1-top). At that time, she was receiving

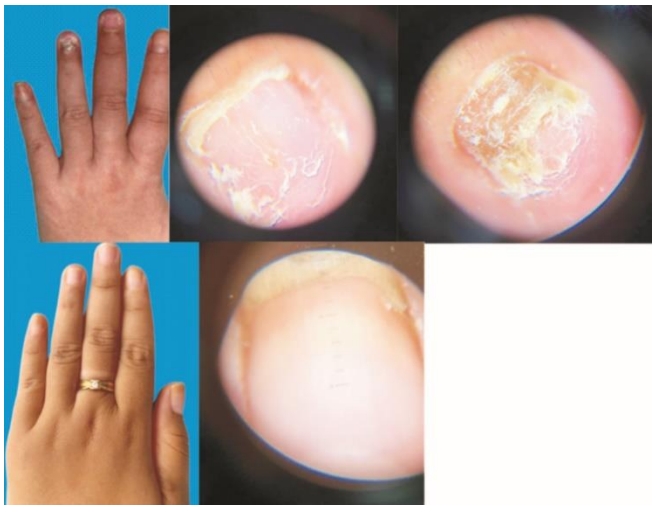

Figure 1: Follow-up images from before (top) and after 4 weeks treatment (bottom) demonstrating clinical improvement following pulsed itraconazole therapy.

methylprednisolone, hydroxychloroquine, cyclosporine, and other supportive medications. While Direct microscopy (KOH preparation) revealed fungal hyphae in fingernails and toenails (Figure 2a). Fungal culture grew two distinct colonies: one with a greenish-yellow velvety surface and rough conidiophores consistent with *Aspergillus flavus* (Figure 2b), and another black colony resembling *Aspergillus niger*. A second culture confirmed *A. flavus* as the dominant pathogen, with no dermatophytes detected. Microscopic examination shows long conidiophores (yellow arrow) and conidia with smooth or slightly rough walls (blue arrow) (Figure 2c).

Based on these findings, the patient was initiated on pulsed itraconazole 400 mg twice daily for 1 week per month. Clinical response was monitored during follow-up visits. On week 1, onycholysis and subungual hyperkeratosis persisted, and hyphae were still observed on KOH examination. By week 2, nail dystrophy and leukonychia were noted, but KOH results were negative. In week 3, white spots remained on the nail surface, with continued negative KOH findings. By week 4, no visible lesions were present, and KOH examination remained negative, indicating both mycological and clinical cure (Figure 1-bottom).

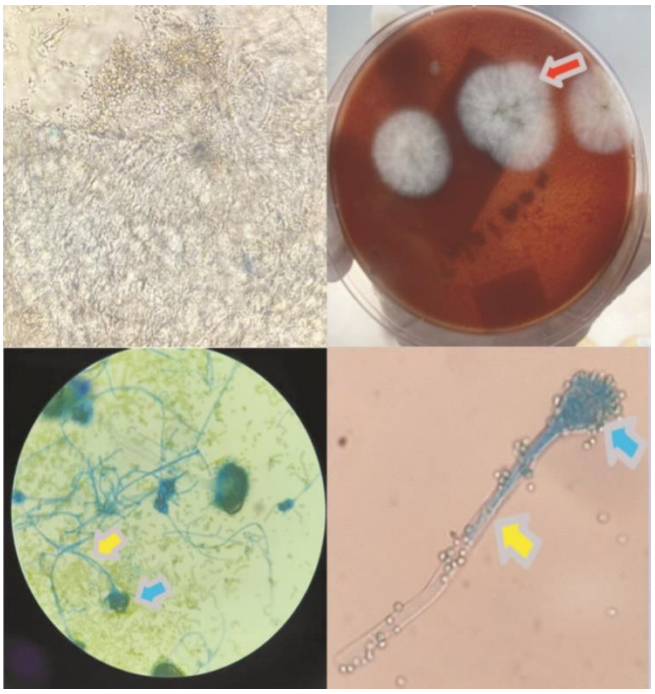

Figure 2: Microbiological examination. (a) Hyphae found on KOH examination of the fingernails. (b) Nail culture showing greenish-yellow velvety surface with white border characteristic of *Aspergillus flavus*.
(c) Microscopy demonstrating long conidiophores (yellow arrow) and conidia with smooth or slightly rough walls (blue arrow).

Discussion

Onychomycosis represents the most prevalent fungal infection affecting nails, accounting for 50–60% of all nail disorders worldwide. It significantly impacts the quality of life due to discomfort, pain, and cosmetic concerns.[1] While dermatophytes are the most common etiologic agents, non-dermatophyte molds (NDMs) like *Aspergillus spp*. are increasingly recognized, especially in immunocompromised patients such as those with systemic lupus erythematosus (SLE).[6] The patient's SLE and immunosuppressive therapy, including corticosteroids and cyclosporine, likely contributed to increased susceptibility to opportunistic fungal infection in the tropical climate of Indonesia. Proximal subungual onychomycosis (PSO), observed in this case, is uncommon and typically associated with immunosuppression. PSO begins at the proximal nail fold and may involve the entire nail plate.[7] It is frequently

caused by *Trichophyton rubrum*, though NDMs have also been implicated.[8]

Aspergillus flavus complex colonies on culture had a characteristic velvety or cottony surface, greenish yellow to olive in color, and often accompanied by yellow spots, and a white border, and on the back, it can be yellow to brown. On microscopic examination, septate hyphae are seen, and the conidiophore is long (400-800 x 8-18 mm), and when fully mature it has a rough or spiny wall, especially in the apex area just below the vesicle.[9] The culture result of this case matches with the characteristic of species, with velvety surface, greenish yellow to olive in color, and white border. And the microscopic result of this case shows long conidiophore, and conidia with smooth and slightly rough walls.

Gupta criteria involve 6 criteria's and NDM can be considered a cause if it fulfills 3 of the following criteria's: (1) KOH examination was positive, fungal elements were found. (2) Nail biopsy shows fungal elements. (3) Culture showed NDMs growth. (4) Repeated cultures showed the same NDMs growth without dermatophyte growth. (5) Culture growth of the same fungus was found in 5 or more than 20 inoculums. (6) NDMs were showed on molecular examination.[3,8] In this case, KOH examination was positive, and 2 culture result showed *Aspergillus flavus*, therefore the criteria were fulfilled.

Treatment of NDM-related onychomycosis is challenging. Antifungal in vitro studies on NDMs showed that *Aspergillus* has the best sensitivity to itraconazole, followed by miconazole, ketoconazole, and terbinafine. Terbinafine 250 mg/day for 1 month or pulsed Itraconazole 400 mg/day for 1 week every month for 2 months can be used for onychomycosis caused by *Aspergillus* infection. In many countries, pulsed itraconazole is approved as a regimen to treat toenail and fingernail onychomycosis by 3-4 pulses. Therapy evaluation may involve mycological cure, clinical cure, and complete cure.[8,10] In this case, complete cure was achieved after three treatment cycles, demonstrating the efficacy of itraconazole in managing Aspergillus onychomycosis.

This case highlights the need for clinicians to consider non-dermatophyte onychomycosis in immunocompromised individuals with atypical nail findings. Accurate identification of the causative pathogen and appropriate antifungal selection are critical for optimal treatment outcomes.

Conclusion

This case demonstrates successful treatment of non-dermatophyte onychomycosis caused by Aspergillus flavus in an SLE patient using pulsed itraconazole. Recognition of atypical presentations and proper mycological workup are important, especially in immunocompromised individuals.

Acknowledgement

We would like to thank the Department of Dermatology and Venereology, Dr. Soetomo General Hospital for the support and facilities provided.

Conflict of Interest: There was no conflict of interest to be declared by any authors.

Funding Source: None.

Author's Contribution

DDS: Conceived, designed, edited the manuscript, given final approval of the version to be published, critical revisions.

MAU: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work.

SS: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work.

EE: Manuscript writing, final approval of the version to be published.

LA: Conceived, designed, edited the manuscript, given final approval of the version to be published, critical revisions.

HM: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work.

TI: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work.

YD: Manuscript writing, final approval of the version to be published.

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