CASE REPORT

Journal of Clinical Microbiology and Infectious Diseases (*JCMID*) 2024, Volume 4, Number 2: 50-53
E-ISSN: 2808-9405

Published By : the Indonesian Society for Clinical Microbiology

Non-dermatophytic onychomycosis caused by *Fusarium spp.* in a 58-year-old agricultural worker: a case report

Sayyidah A. Aminy[1], Devika N. Amaia[2], Hardyanto Soebono[2], Titik Nuryastuti[1*]

[1]Microbiology Department, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia;
[2]Department of Dermatology and Venereology (DV), Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.

*Corresponding to:
Titik Nuryastuti;
Microbiology Department, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia;
t.nuryastuti@ugm.ac.id

Received: 2023-09-26
Accepted: 2024-11-25
Published: 2024-12-13

ABSTRACT

Introduction: Onychomycosis is a nail infection caused by dermatophytes, non-dermatophytes, and yeast. *Fusarium spp*. is one of the non-dermatophyte molds that can cause onychomycosis. A superficial infection with these fungi can lead to an invasive infection. Few case reports of onychomycosis caused by *Fusarium spp.* in Indonesia have been documented.
Case description: We present a case of a 58-year-old male patient with a history of hepatitis B, atopic dermatitis, and corticosteroid consumption. Hyperkeratosis with a yellowish color was observed, and small particles of cornified material were discovered beneath both of his great toenails. Onychomycosis is assessed based on clinical symptoms. Mycological examinations were done by KOH examination and culture. Macroscopic examination of the culture revealed a white, cottony-looking mold with a non-pigmented reverse. Microscopic examination showed the septate hyphae, the canoe-shaped macroconidia, and the oval microconidia. We diagnosed onychomycosis caused by *Fusarium spp.* Based on macroscopic and microscopic examination. The antifungal susceptibility test showed a high MIC against several antifungal agents.
Conclusion: It is important to be cautious for onychomycosis caused by *Fusarium spp.* infection as superficial infection can progress to invasive disease. Given the high prevalence of *Fusarium spp.* resistance to the antifungal group, antifungal treatment selection should be carefully considered.

Keywords: *agricultural worker, non-dermatophytic onychomycosis, Fusarium spp*.
Cite This Article: Aminy, S.A., Amaia, D.N., Soebono, H., Nuryastuti, T. 2024. Non-dermatophytic onychomycosis caused by *Fusarium spp*. in a 58-year-old agricultural worker: a case report. *Journal of Clinical Microbiology and Infectious Diseases* 4(2): 50-53. DOI: 10.51559/jcmid.v4i2.66

INTRODUCTION

Onychomycosis is a fungal infection of the nails that can affect both toenails and fingers.[1] Symptoms may include nail discoloration, thickening of the skin beneath the nails (subungual hyperkeratosis), detachment of the nail from its bed (onycholysis), splitting of the nail plate, and nail plate disintegration.[2] Onychomycosis is the most common nail problem, accounting for at least half of all nail diseases. It can caused by dermatophytes (60-70%), non-dermatophytes (10%), or yeast (20%).[3,2] Some risk factors for onychomycosis include dermatologic diseases such as tinea pedis, psoriasis, diabetes mellitus, immunosuppressive conditions, chronic venous insufficiency, peripheral artery disease, obesity, and nail injury.[1,2] Onychomycosis affects 3-26% of individuals globally, indicating that this illness is a serious health concern.[4]

Non-dermatophyte molds like *Aspergillus, Fusarium, Acremonium,* and *Alternaria* contribute to approximately 10 percent of onychomycosis cases worldwide.[1,3] *Fusarium spp.* is a non-dermatophyte fungal that can cause onychomycosis with trauma, contact with soil, and agricultural occupation as risk factors.[5-6] Some species in this genus are pathogenic to humans, like *F. solani* species complex, *F.* oxysporum species complex, *F.* fujikuroi species complex, *F. incarnatum equiseti* species complex, and *F.* dimerum species complex.[7] *Fusarium spp.* definitive identification of these species complexes requires molecular examination.[7] species have been identified as plant pathogens that inhabit soil and may be found worldwide.[5] Onychomycosis caused by *Fusarium* can also become a source of invasive infectious agents for other body regions and, especially in immunocompromised persons.[1,8] *Fusarium*-related onychomycosis is generally difficult to treat due to its resistance to several antifungals.[1]

There are still a few cases reported of onychomycosis caused by *Fusarium spp.* in Indonesia. We reported a case of onychomycosis in a 58-year-old man that was caused by non-dermatophyte fungi *Fusarium spp.*

CASE DESCRIPTION

A 58-year-old man presented himself at the Dermatology and venereology outpatient clinics of RSUP Dr. Sardjito with suspected distal lateral subungual onychomycosis on his right great toenails. The patient's great toenails had hyperkeratosis with a yellowish color, and small particles of cornified material were discovered beneath the nail. This complaint has been felt for the last few years. The patient had a history of allergic contact dermatitis for the last 3 years, with complaints of itching and redness, especially in his hands and legs. A history of urticaria caused

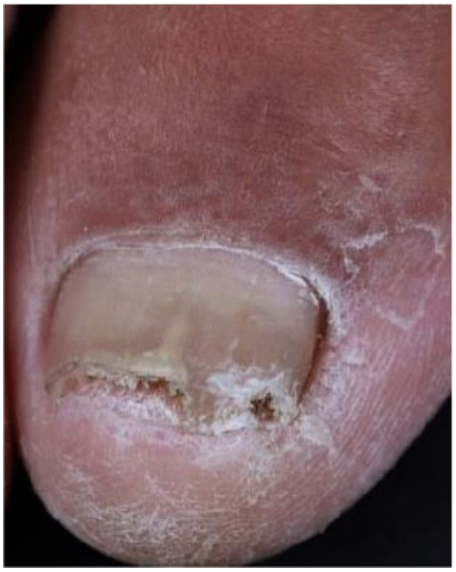

Figure 1. Clinical features of the toenail lesion caused by *Fusarium spp.* Nail discoloration with a subungual hyperkeratosis was observed.

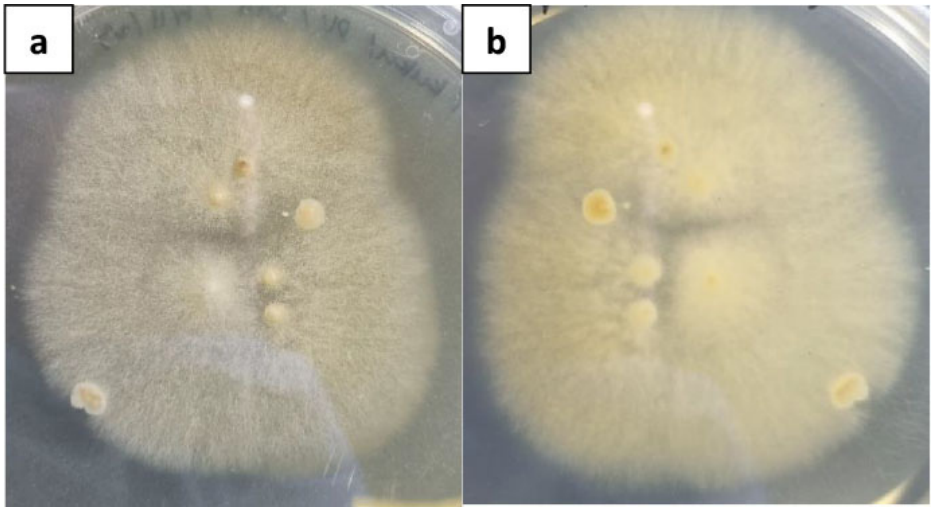

Figure 2. The macroscopic examination showed a white cottony appearance from several points of specimens (a) with non-pigmented reserve (b).

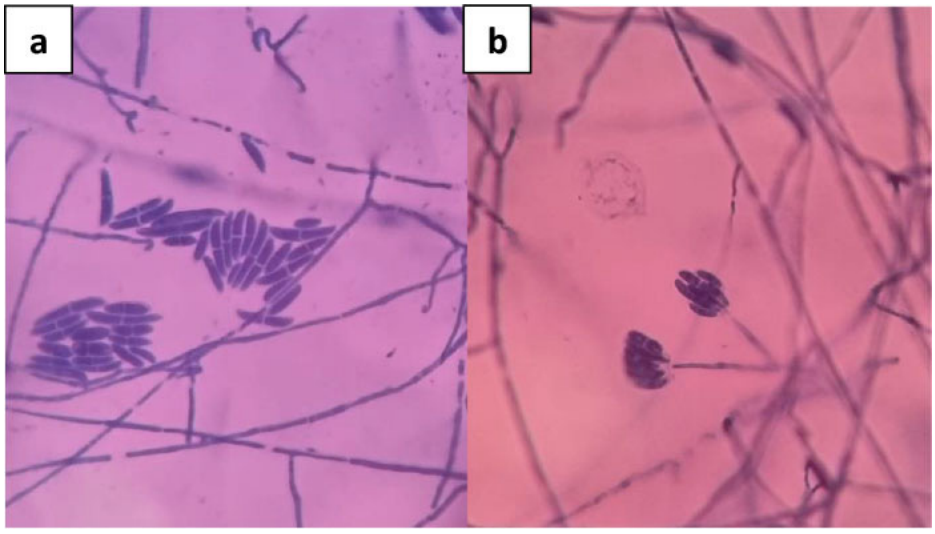

Figure 3. The microscopic examination (a,b) showed examination showed the septate hyphae, the canoe-shaped macroconidia, and the microconidia.

Table 1. In vitro susceptibility of *Fusarium spp.* Isolate against four antifungal drugs using broth microdilution methods

Antifungal	MIC (µg/mL)	Drug breakpoints (µg/mL)*
Ketoconazole	>32 µg/mL	-
Itraconazole	>64 µg/mL	-
Fluconazole	>64 µg/mL	-
Terbinafine	>32 µg/mL	-

Note: *Drug breakpoints for molds for *Fusarium spp.* are still not defined by CLSI M38 (2017) and EUCAST (2020)

by eating eggs was found. The patient denies having a history of asthma and allergic rhinitis but has a positive atopic history from his grandfather. The patients frequently use corticosteroid drugs to treat allergic contact dermatitis. He works as an agricultural worker in an oil palm plantation with a history of nail trauma while working in the field. Onychomycosis is assessed based on clinical symptoms.

Nail-scraping and subungual nail debris specimens were collected from the patient's great toenails using a sterile nail clipper for microbiological analysis. The specimens were cultured into both Sabouraud Dextrose Agar Medium (SDA) supplied with chloramphenicol with and without cycloheximide. The specimens were then incubated at 35°C. Direct microscopic examination with KOH 10% was done using the remaining specimens, but no fungal elements were found. The growth rate of the cultures was checked daily for one week for identification. On the third day of incubation, the growth of mold colonies was observed from all inoculated points and media (figure 1). According to macroscopic examination, a white cottony appearance mold with non-pigmented reverse was found. Microscopic examination showed the septate hyphae, the canoe-shaped macroconidia, and the microconidia (figure 2). There was no dermatophyte growth from Sabouraud dextrose agar media with cycloheximide supplementation. According to macroscopic and microscopic examinations, the fungi was identified as *Fusarium spp.* In this case, no other laboratory tests were conducted. Clinical symptoms, including nail hyperkeratosis, discoloration, and brittleness, supported by the phenotypic identification of *Fusarium spp*. from culture examination, confirmed the diagnosis of *Fusarium* Onychomycosis. The patient was treated with terbinafine 250 mg/day for 6 weeks. Whereas, onychomycosis caused by

Fusarium spp. is challenging to treat due to its resistance to many classes of antifungals.

Antifungal susceptibility test with microdilution method was done and was interpreted according to the third edition of M38; Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi, published by the Clinical and Laboratory Standards Institute (CLSI). RPMI 1640 medium (Sigma-Aldrich) with glutamine, without bicarbonate, and with phenol red as a pH indicator was used as the culture medium. The isolate was incubated in Sabouraud dextrose agar for at least 48 hours at 35°C before the susceptibility test to induce conidium and sporangiospore formation. Suspension of the isolate was prepared, and 0.85% saline was equal to 0.5 mc Farland. The growth control wells contain 0.1 mL of diluted isolate suspension and drug diluent without an antifungal agent. Then, the microdilution plate was incubated at 35°C for 48 hours before interpretation. From in vitro antifungal susceptibility tests that were done, the Minimum Inhibitory Concentration of the isolate against four antifungal drugs were Ketoconazole (MIC >32 µg/mL), Itraconazole (MIC >64 µg/mL), Fluconazole (MIC >64 µg/mL) and Terbinafine (MIC >32 µg/mL).

DISCUSSION

Dermatophytes, Non-Dermatophyte Molds (NDM), and/or yeast are the most common causes of onychomycosis. Onychomycosis caused by NDM accounts for 1.45%-17.6% of all cases, with *Fusarium spp.* being one of the etiological agents.[9,10] *Fusarium spp.* causes 9-44% of non-dermatophyte molds (NDM) onychomycosis.[11] Trauma, contact with soil, barefoot walking, and work in agriculture are several risk factors that cause *Fusarium* onychomycosis.[6] *Fusarium spp.* are not keratolytic. Therefore, they infect the nail plate and survive on nonkeratinized intercellular cement that has been injured by trauma.[10]

Toenails are more likely to be affected by NDM onychomycosis than fingernails due to repetitive damage, slower growth, thicker nail plates, constant exposure to moist environments, and reduced blood flow to underlying tissues. Indonesia is a tropical country with a hot and humid climate, which increases the risk of onychomycosis.[1,10]

In those with risk factors, onychomycosis can cause not only cosmetic changes and discomfort to nails. Still, it may additionally act as a source of more serious infection in other parts of the body.[1] Fusarium's intrinsic resistance to numerous antifungal drugs usually leads to poor treatment outcomes for patients.[6] A few variables like the severity of nail involvement, presence or absence of tinea pedis, treatment efficacy, and potential adverse effects determine the management of onychomycosis. Three treatment modalities that may be considered are systemic therapy, topical therapy, and mechanical intervention.[12]

This case report explained onychomycosis in a 58-year-old man caused by *Fusarium spp.* As we know, *Fusarium spp.* can be found in an environmental, which could be a contaminant in clinical nail samples. Appropriate sampling, specimen handling, and inoculating in several plates and points at Saboraoud dextrose agar are required to determine this fungal as a pathogen. Gupta et al. suggested applying three of their six clinical guideline criteria: KOH identification, isolation in culture, repeated isolation, inoculum counting, dermatophyte exclusion, and histological proof or NDM identification using genetic techniques. This case report met three of the six criteria: isolation in culture, inoculum counting, and dermatophyte exclusion, which reinforced *Fusarium spp.* as a pathogen.[6,10]

Fusarium spp. is a fast-growing mold that matures in four days. It has a white cottony colony with a light reserve. *Fusarium spp*. possesses septate hyphae and macroconidia that are canoe-shaped with three to five septate and oval microconidia. The isolate was identified as *Fusarium spp,* through macroscopic and microscopic testing.

Treatment of *Fusarium spp.* infection is complicated due to intrinsic resistance to azole, echinocandins, and polyenes antifungals and the rise of multidrug-resistant strains as a result of agricultural antifungal misuse.[1,6] There are currently no clinical breakpoints for antifungal drugs that target various *Fusarium* species, either according to CLSI or EUCAST standards.[6] Limited data are available to suggest a correlation between MIC and treatment outcome with triazole antifungal class and *Fusarium spp.*[8] However, antifungal susceptibility testing is important as part of periodic batch surveys to establish an antibiogram for pathogenic organisms within a healthcare facility, to help with the management of invasive and cutaneous infections caused by molds when the efficacy of an antifungal agent is unknown, and for patients who have had prior exposure to an antifungal class or who have received prolonged antifungal treatment.[8] But caution should be used when interpreting the minimal inhibitory concentration (MIC) results for any molds/drug combination.[8] Minimal inhibitory concentration (MIC) is the lowest concentration of an antimicrobial agent that causes a specified reduction in the visible growth of a microorganism in an agar or broth dilution susceptibility test.[8] However, until now, there are no guidelines to indicate a correlation between MIC and the outcome of treatment with ketoconazole, Itraconazole, and terbinafine.[8]

In a study conducted by Lu et al. (2023), the range of MICs of in-vitro antifungal susceptibility test from *Fusarium spp.* against antifungal agents was quite high, with the MIC range for Terbinafine 2 µg/mL –>32 µg/mL, Fluconazole >64 µg/mL, Ketoconazole, Itraconazol 4 µg/mL ->32 µg/mL.[6] In accordance with this, 53.8% of *Fusarium spp.* onychomycosis patients responded poorly to the antifungal medication they received.[6] It is similar to the results of antifungal susceptibility testing of this case report isolate. The range of MICs was relatively high, MIC range for Terbinafine, Fluconazole, Ketoconazole, and Itraconazole were >64 µg/mL, >64 µg/mL, >32 µg/mL, and >32 µg/mL, respectively. Based on the MICs data, the optimal treatment options for this case remain limited and challenging.

This study has several limitations. First, the patients terminated follow-up, rendering it unable to evaluate the outcomes of the administered therapy, both clinically and mycologically. Second, the causative pathogen was identified

phenotypically, which restricted species-level identification. Third, no molecular or histological studies were carried out in this study to support the diagnosis.

CONCLUSION

We reported a case of non-dermatophyte onychomycosis in an agricultural worker caused by *Fusarium spp.* The *Fusarium* has a high MIC for all antifungals that have been tested, although the clinical breakpoint of *Fusarium spp.* has not been determined by CLSI; the high MIC indicates *Fusarium spp.* resistance to several antifungals, which can complicate therapy. It is important to be aware of *Fusarium spp.* infection since it can lead to disseminated and invasive infection, particularly in those with risk factors with poor response to empirical antifungals. Given the high prevalence of fusarium resistance to the antifungal group, the choice of antifungal medicines utilized should be carefully considered.

DISCLOSURES

Funding
No funding.

Conflict of Interest
There is no conflict of interest in this study.

Consent for Publication
Written informed consent was obtained from the patient's parent to publish this case report in an academic journal and any accompanying images.

Author Contribution
Conceptualization, methodology and writing original draft preparation: Aminy S.A.; Data collection: Amalia, D.N.; Writing, review, and editing: Aminy S.A., Amalia, D.N., Nuryastuti T., Soebono H.; Approval of final manuscript: all authors

REFERENCES

1. Cañete-Gibas C, Wiederhold NP. Mycology of Onychomycosis. Clin Microbiol Newsl [Internet]. 2023;45(2):11–7. Available from: http://dx.doi.org/10.1016/j.clinmicnews.2023.01.002
2. Maskan Bermudez N, Rodríguez-Tamez G, Perez S, Tosti A. Onychomycosis: Old and New. J Fungi. 2023;9(5):1–13.
3. Leung AKC, Lam JM, Leong KF, Hon KL, Barankin B, Leung AAM, et al. Onychomycosis: An Updated Review. Recent Pat Inflamm Allergy Drug Discov. 2019;14(1):32–45.
4. Grover C, Khurana A. Onychomycosis: Newer insights in pathogenesis and diagnosis. Indian J Dermatol Venereol Leprol. 2012;78(3):263–70.
5. Uemura EVG, Barbosa MDS, Simionatto S, Al-Harrasi A, Al-Hatmi AMS, Rossato L. Onychomycosis Caused by Fusarium Species. J Fungi. 2022;8(4):7–18.
6. Lu LY, Ou JH, Hui RCY, Chuang YH, Fan YC, Sun PL. High Diversity of Fusarium Species in Onychomycosis: Clinical Presentations, Molecular Identification, and Antifungal Susceptibility. J Fungi. 2023;9(5).
7. Larone D, Westblade LF, Burd EM, Lockhart SR, Procop GW, Walsh TJ. Larone's Medically Important Fungi: A guide to identification (7th edition). 7th editio. American Society for Microbiology; 2023.
8. Alexander BD, Clinical and Laboratory Standards Institute. Reference method for broth dilution antifungal susceptibility testing of filamentous fungi. Vol. 3. 2018. 50 p.
9. Kim DM, Suh MK, Ha GY, Sohng SH. Fingernail onychomycosis due to Aspergillus niger. Ann Dermatol. 2012;24(4):459–63.
10. Gupta AK, Summerbell RC, Venkataraman M, Quinlan EM. Nondermatophyte mould onychomycosis. J Eur Acad Dermatology Venereol. 2021;35(8):1628–41.
11. Diongue K, Ndiaye M, Seck MC, Diallo MA, Badiane AS, Ndiaye D. Onychomycosis Caused by Fusarium spp. in Dakar, Senegal: Epidemiological, Clinical, and Mycological Study. Dermatol Res Pract. 2017;2017:1–5.
12. Christopher PM, Winaya KK. Onychomycosis Caused by Aspergillus niger : A Case Report of An Unusual Etiological Agent. 2022;11(1):2020–3.