Case Report
Olgu Sunumu

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A case of onychomycosis caused by *Aspergillus niger*

Aspergillus niger'in neden olduğu bir onikomikoz olgusu

Seher Bostancı, Bengü Nisa Akay, Merve Alizada*, Aylin Okçu Heper**, Ebru Evren***

Ankara University Faculty of Medicine, Department of Dermatological and Venereal Diseases, Ankara, Türkiye
*Mamak Hospital, Clinic of Dermatological and Venereal Diseases, Ankara, Türkiye
**Ankara University Faculty of Medicine, Department of Medical Pathology, Ankara, Türkiye
***Ankara University Faculty of Medicine, Department of Medical Microbiology and the Ibni Sina Hospital Center Microbiology Laboratory, Ankara, Türkiye

Abstract

Between 2015 and 2018, a clear increase was noticed in the cases of onychomycosis in which species of Aspergillus were cited as the cause while stimulating studies have been conducted. With this case, we call attention to the increasing frequency of Aspergillus niger onychomycosis in recent years and highlight the options for diagnosis and treatment as well as the risk factors and clinical and pathological properties of the disease.
Keywords: Onychomycosis, *Aspergillus niger*, treatment

Öz

Çalışmalar, 2015-2018 yılları arasında Aspergillus türlerinin sebep olduğu onikomikoz olgularında belirgin artışa dikkat çekmiştir. Biz de olgumuzla Aspergillus niger onikomikozunun son yıllarda artan sıklığına dikkat çekmeyi, tanı ve tedavi seçenekleri ile hastalığın risk faktörleri ile klinik ve patolojik özelliklerini vurgulamayı amaçladık.
Anahtar Kelimeler: Onikomikoz, *Aspergillus niger*, tedavi

Introduction

Non-dermatophyte fungi (NDF), including *Scopulariopsis, Aspergillus* and *Fusarium* species, and candida are found to be causative agents in 2-25% of onychomycosis cases, which are often caused by dermatophytes[1]. In recent years, *Aspergillus species* have been increasingly encountered as the cause of onychomycosis[2-4]. With our case of onychomycosis caused by *Aspergillus niger*, we aimed to draw attention to the increasing frequency of *Aspergillus* spp. associated onychomycosis cases in recent years, and to emphasize the risk factors, clinical and pathological features, as well as the diagnosis and treatment options of the disease.

Case Report

An 89-year-old immunocompetent female patient with diabetes and hypertension was referred to us with complaints of developing color changes in the nail on her left hallux for four months. She had no history of trauma and cold sensitivity.

Address for Correspondence/Yazışma Adresi: Merve Alizada MD, Mamak Hospital, Clinic of Dermatological and Venereal Diseases, Ankara, Türkiye
Phone: +90 533 424 22 89 **E-mail:** werve2007@gmail.com **Received/Geliş Tarihi:** 23.05.2023 **Accepted/Kabul Tarihi:** 23.10.2023
ORCID: orcid.org/0000-0003-2732-9132

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The physical examination revealed white color changes in the nail on her left hallux, sporadic areas verging on purple in the nail, black color changes under the nail plate, a light subungual hyperkeratosis in the proximal nail, sporadic thinning in the nail plate, erythema around the nail, and sensitivity in the nail (Figure 1a).

In laboratory tests, the HbA1C of the patient was determined to be 7.5%, with normal complete blood cell count, and C-reactive protein values. HIV and hepatitis serology were negative.

In the direct microscopic examination of nail samples with potassium hydroxide (KOH), no dermatophytes were detected and a nail fold biopsy was taken. The black pigment was noted beneath the nail and in the nail fold during the biopsy, and pathological and microbiological samples were taken from the region (Figure 1b). In the pathological examination, a portion of the pigment, numerous spores, and sparse hyphae form fungi were determined in groups among the keratin lamellae in the sections. The spores and hyphae were stained with Grocott methenamine silver (GMS) and periodic acid-Schiff (PAS), and the septate hyphae were monitored in the GMS stain in the sample for the nail plate (Figure 1c). The samples obtained from the formation of black pigments were cultured at 25 °C in sabouraud dextrose agar and potato dextrose agar, and numerous similar black colonies were seen in the stock at the 24th hour. Reproducing colonies were observed with lactophenol cotton blue microscopically, and were typified as *Aspergillus niger* with matrix-assisted laser desorption/ionization-time-of-flight mass spectrometer (Bruker Daltonics, Germany) (score ≥2) (Figure 1d).

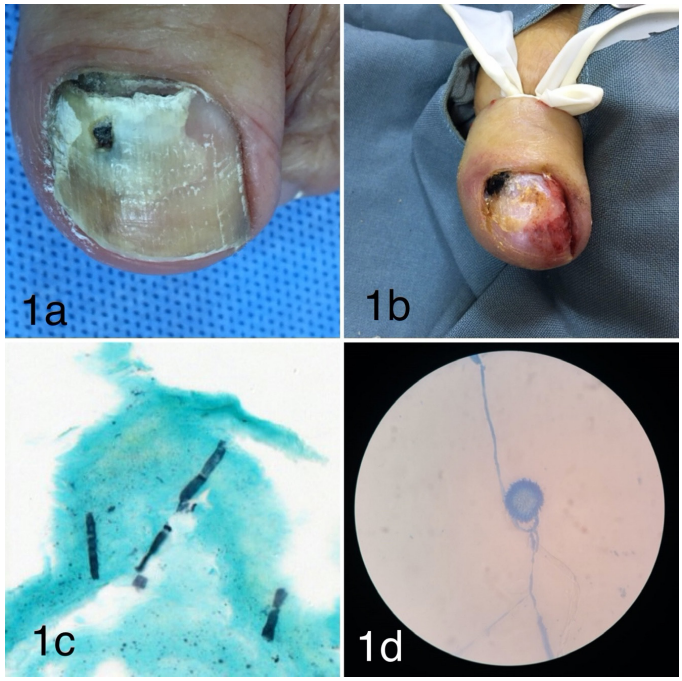

Figure 1. (a) White color changes in the nail on her left hallux, black color changes under the nail plate, a light subungual hyperkeratosis in the proximal nail, thinning in the nail plate, and erythema around the nail, **(b)** The black pigment forms in the nail fold during the biopsy, **(c)** (GMSx18.4) Septal, non-branching hyphae in the sample for the nail shaft on histopathological examination, **(d)** (x40) Microscopic image of the culture samples stained with lactophenol cotton blue

After *Aspergillus niger* was detected in the nail culture of the diabetic patient, the infection clinic started IV micafungin treatment for the patient. The patient received intravenous micafungin treatment on the 10th day of hospitalization. During the follow-up, it was determined that the patient did not have systemic *Aspergillus* infection but had isolated onychomycosis. IV micafungin treatment was discontinued and she was successfully treated with 200 mg/day of oral itraconazole and topical ciclopirox olamine citrate. Informed consent was obtained.

Discussion

Aspergillus spp. is a notable cause of onychomycosis that has been gradually increasing in frequency in recent years[2]. It is determined as the cause in approximately 35% of onychomycosis cases in Guatemala and is found in onychomycosis etiologies in up to 71% of diabetic patients[5]. *A. flavus*, *A. terreus*, and *Aspergillus niger* are the most frequently identified species[5]. The *Aspergillus* subspecies *Aspergillus niger* was determined most frequently in studies conducted in diabetic patients[4]. Advanced age, hyperhidrosis, trauma, immunosuppression, paronychia, diabetes, HIV, and immunosuppression have been shown as risk factors. *Aspergillus* spp. has been reported as the cause of onychomycosis in both immunosuppressed and healthy individuals[6]. To the best of our knowledge, there are six cases of *A. niger* onychomycosis reported in the literature. In our case, the 89-year-old female patient with diabetes had a history of paronychia, and *Aspergillus niger* was determined as the cause of onychomycosis.

In cases of onychomycosis caused by *Aspergillus* spp. that naturally produces pigments of different colors, subungual hyperkeratosis is observed with black, blue, brown, and green color changes. The infection begins beneath the nail, spores settle on the hyponychium, lateral fold, and nail plaque and multiply, and the infection spreads toward the cuticle. As with dermatophytes, it leads to thinning and fractioning in the nail[5]. It is difficult to differentiate clinically between *Aspergillus* spp. and dermatophytes because of similar findings. Proximal subungual onychomycosis (PSO) requires a microbiological examination for definitive diagnosis, even though white color changes in the nail, absence of discharge, painful paronychia, and the observance of rapid lamina invasion have been correlated to *Aspergillus* onychomycosis[7]. In our case, sensitivity in the nail, paronychia without discharge with periungual erythema, white color changes, and PSO, seen as sporadic black spots, were present. The melanin produced by *Aspergillus niger* caused the specific, black pigmentation observed beneath the nail plaque and nail fold during the biopsy. Some strains of *T. rubrum* and *A. tubingensis* cause melanonychia like *Aspergillus niger*. *Aspergillus niger* onychomycosis is included in the differential diagnosis in other types of onychomycosis, psoriasis, paronychia, and nail fold tumors because of their clinical properties. *Aspergillus* spp. can cause onychomycosis in nail fold tumors[8]. In our case, a pathological examination was done from the nail fold. Should *Aspergillus niger* be determined as the cause of onychomycosis, which is quite rare, nail fold biopsy is recommended, as this procedure can guide the clinician in determining the accompanying nail fold pathology.

Microbiological tests are important to differentiate *A. niger* onychomycosis from colonization and contamination[9]. Diagnostic methods used include:

Direct microscopic examination: KOH is used to identify fungal elements such as hyphae, mycelium, and arthrospores, with dermatophytes easily distinguished.

Fungal culture: This method confirms clinical suspicion and assesses pathogen viability, identifying molds based on microscopic and macroscopic colony characteristics such as color, texture, and pigmentation[9,10].

Histology: Using PAS or haematoxylin and eosin staining, histology visualises fungal elements in nail clippings, providing high sensitivity but no insight into the nature or viability of the organism[1].

Molecular biology techniques: Newer methods use polymerase chain reaction (PCR) to amplify fungal DNA, targeting specific genes such as beta-tubulin and actin[1,3,11]. For example, beta-tubulin is used in the detection of *Aspergillus* spp.[11]. For non-dermatophyte molds (NDMs), unique genetic targets are utilized. Nested PCR is employed for the detection of various fungi, including NDMs such as *Aspergillus* spp.

Gupta et al.[3] established six criteria for diagnosing exclusive NDM onychomycosis: Direct microscopy using a KOH preparation, mold isolation in culture, repeated mold isolation in culture, inoculum counting, dermatophyte exclusion in culture (absence of dermatophyte growth), histological examination. The presence of at least three of these criteria was recommended for a more accurate diagnosis of NDM[3,9,10]. Another study proposed a modified diagnostic approach for the detection of onychomycosis. If mold is initially detected in a nail sample from a suspected patient, three additional nail samples are cultured during follow-up visits[12]. Confirmation of mold as the true onychomycosis pathogen occurs when all three samples show identical mold growth.

Although some studies show that itraconazole is more effective than terbinafine in the treatment of *Aspergillus* onychomycosis under *in vitro* conditions, it has been reported that treatment with terbinafine 250 mg daily and pulsed itracanazole 400 mg daily for 1 week per month showed similar efficacy[7]. In our patient, systemic micafungin treatment was given primarily for systemic *Aspergillosis* infection, but when the infection was found to be localized to the nail, it was replaced with systemic itraconazole treatment[11,13]. Systemic antifungals, keratolytic preparations containing 40% urea, and ciclopirox olamine nail polish are recommended as the ideal treatment combination[7]. Topical efinaconazole, luliconazole and systemic voriconazole, posaconazole and topical or systemic amphotericin B can also be used for treatment[11].

In conclusion, clinical, pathological, and microbiological methods and diagnostic criteria are important in the diagnosis of *Aspergillus* onychomycosis, notable for its recent increasing frequency.

Ethics

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.O.H., Design: A.O.H., Data Collection or Processing: S.B., B.N.A., M.A., A.O.H., E.E., Analysis or Interpretation: S.B., B.N.A., M.A., A.O.H., E.E., Literature Search: S.B., B.N.A., M.A., A.O.H., E.E., Writing: S.B., B.N.A., M.A., A.O.H., E.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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