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Case Report

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Presentation of Like Melanoma Onychomycosis Due to Fusarium Solani Species Complex

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1. Abstract

Onychomycosis is a fungal infection of the nail caused by molds, yeasts and dermatophytes. In this study, we report a case with unusual fingernail onychomycosis in a 31-year-old Iranian woman suspected having nail bed melanoma. Biopsy was performed from the nail bed and no any evidence of melanoma was reported by the pathologist. In Direct Microscopic Examination (DME) and culture numerous hyaline septated hyphae and canoe-shaped conidia on conidiophores were observed, respectively. Diagnosis was confirmed by molecular DNA sequencing and Fusarium solani species complex was identified as etiological microorganism.

2. Introduction

Onychomycosis is a fungal infection of finger or toenails resulting from the invasion of dermatophyte, yeast or mold species to the nail plate [1]. The most important non-dermatophyte molds causing onychomycosis are Scopulariopsis brevicaulis, Fusarium spp, Aspergillus spp, Acremonium spp [2, 3]. Fusarium species distributed worldwide, causing, onychomycosis and commonly found in nature, both as soil saprophytes and plant pathogens [4]. In the healthy individuals, superficial infection of the eye, skin and nail due to Fusarium are less common. The infection is usually precipitated by predisposing factors such as traumatic tissue damage, dystrophic abnormalities, diabetes, neutropenia, cortichosteroid therapy, HIV infection, hematological malignancies and other immunosuppressive conditions [5-7]. Fusarium onychomycosis usually involved the great toenail and white superficial onychomycosis have been reported as typical clinical form, but proximal subungual onychomycosis with acute or sub acute paronychias have been reported by the others8. Here, we report a severe fingernail infection caused by Fusarium solani complex that was similar to melanoma lesion.

3. Case Report

In May 2016, a 31-year-old woman with deformity and black discoloration right middle finger nail with paronychia was referred to Mycology Research Center, Faculty of Veterinary Medicine, University of Tehran, Iran (Figure 1a). She suffered from pain and discharge around the infected nail. Regarding the clinical signs, it was suggested as melanoma but in histology of nail biopsy melanoma was not confirmed. Routine laboratory analyses of blood and urine were normal and she did not have any underlying disease or immune disorders. In biopsy, massive lamellar orthokeratosis, parakeratosis and basophilic granular (mycetoma-like) colonies with sepated and hyalin hyphae were observed. Samples were obtained from the proximal and distal portions of the affected nail by clip-

ping and scraping of the debris. In direct DME narrow and septated hyphae in the nail sample were observed (Figure 1a, 1b). Into sabouraud culture, cottony white colony that was yellow orange on the reverse side were grown (Figure 1e, 1f). Culture revealed irregular and fine septated hyaline hyphae and micro/macro conidia which compatible with Fusarium species (Figure 1c, 1d). Hyphae were also observed in histopathologic sections of the nails Samples (Figure 2). Histopathological examination of a biopsy also showed massive lamellar orthokeratosis and parakeratosis. Moreover, numerous basophilic granular colonies (mycetoma-like) admixed with thick hyphae – like of fungal elements which were surrounded by inflammatory cells and a few scattered small masses of epithelial cells throughout the sample were observed (Figure 2). Histopathological findings of a soft tissue biopsy showed hyperplastic epithelium overlying thick hyperkeratosis (Figure 2). Satisfied feature of malignancy was not seen in these submitted samples. Species identification was accomplished by molecular identification. Fungal strains were grown on Potato Dextrose Agar (PDA) plates for 5 days at room temperature and genomic DNA was extracted Based on Liu methodology [9].

Amplification of TEF gene region, which is used for phylogenetic study of Fusarium species, was performed by universal primers as follows: ef1 (forward primer; 5-ATGGGTAAGGA(A/G) GACAAGAC-3) and ef2 (reverse primer; 5-GGA(G/A)GTAC-CAGT(G/C)ATCATGTT3 [10,11]. The reaction mix was performed in a volume of 50µL containing 0.5 µM of each primer, 0.2 µM of each deoxynucleoside triphosphate, 5µl of 10×PCR buffer (Applied Biosystems), 2.5 U Taq DNA polymerase (Amplitaq; Applied Biosystems), and 25 ng of DNA. The PCR protocol was: 95°C for 5 min; then 30 cycles of 20s at 95°C, 40s at 54°C, and 60s at 72°C; and a final cycle at 72°C for 5 min. PCR amplified products were purified by QIA quick Gel Extraction Kit (Qiagen, Valencia, CA, USA) and then conducted for sequencing service with the EF1 primer in two directions by Takapouzist Co. (Bioneer, Republic of Korea). The sequences were edited by Chromas and the resulting sequence was served as a query to search for similarities. Therefore, the BLAST network services at the National Centre for Biotechnology Information (http://www.ncbi.nlm.nih.gov/NCBI) were used and according to the result F. solani species complex (NRRL32542; MLST type: 3+4-ii) DQ247008 was identified (Figure 3).

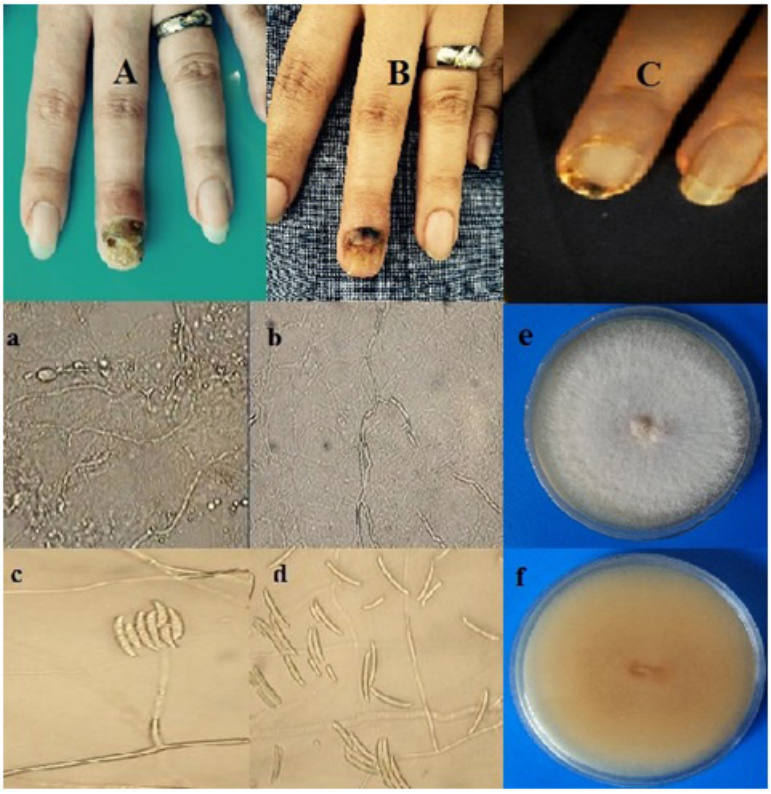

Figure 1: (A) Right middle finger nail at first clinical observation: Deformity, discoloration and periungual inflammation around the nail plate (B) Affected nail plate after surgical debridement (C) During treatment. (a, b) Septated and narrow hyaline hyphae in DME (X 40). (c, d) macro-conidia of Fusarium with 2-5 chambers in slide culture, (e, f) culture of nail samples on SCC agar. Cottony-white colony that was yellow-orange on the reverse side.

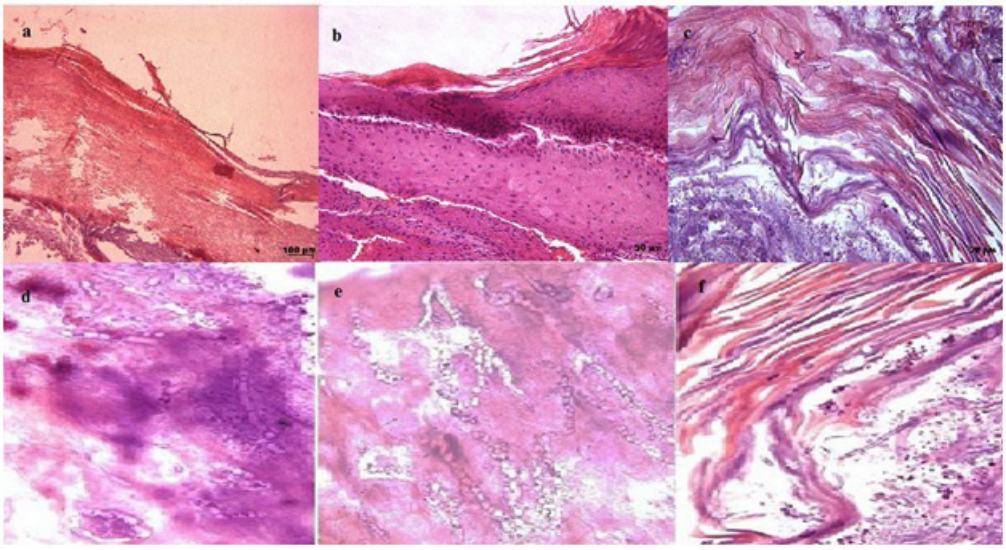

Figure 2: Histopathology of affected nail: Massive lamellar orthokeratosis and parakeratosis (a, b and c). Fungal hyphae in histopathology sections of the nails samples (d,e and f).

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Reference sequence:
F. solani species complex (NRRL 32542; MLST type: 3+4-11) DQ247008
F. falciforme, F. solani species complex, N1: Translation elongation factor 1 alpha gene (EF1) Sequence
length: 668
Similarity: 667/668 [99.850 %], Gaps: 1 [0.150 %], Coverage: 667/668 [99.850 %] Score:
1036.57, Probability: 0, Direction: +/+

Qry 1           TCGTCGTCATCGGCCACGTCGACTCTGGC-AGTCGACCACCGTAAGTCAAACCCTCATCG 59
                ||||||||||||||||||||||||||||| ||||||||||||||||||||||||||||
Ref 1           TCGTCGTCATCGGCCACGTCGACTCTGGCAAGTCGACCACCGTAAGTCAAACCCTCATCG 60

Qry 60          CGATCTGCTTATCTCGGGTCGTGGAACCCCGCCTGGCATCTCGGGCGGGGTATTCATCAG 119
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 61          CGATCTGCTTATCTCGGGTCGTGGAACCCCGCCTGGCATCTCGGGCGGGGTATTCATCAG 120

Qry 120         TCACTTCATGCTGACAATCATCTACAGACCGGTCACTTGATCTACCAGTGCGGTGGTATC 179
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 121         TCACTTCATGCTGACAATCATCTACAGACCGGTCACTTGATCTACCAGTGCGGTGGTATC 180

Qry 180         GACAAGCGAACCATCGAGAAGTTCGAGAAGGTTGGTGACATCTCCCCCGATCGCGCCTTG 239
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 181         GACAAGCGAACCATCGAGAAGTTCGAGAAGGTTGGTGACATCTCCCCCGATCGCGCCTTG 240

Qry 240         CTATTCCACAACGAATTCCCTCCCTCGCGATACGCTCTGCGCCCGCTTCTCCCGAGTCCC 299
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 241         CTATTCCACAACGAATTCCCTCCCTCGCGATACGCTCTGCGCCCGCTTCTCCCGAGTCCC 300

Qry 300         AAAATTTTTGCGGTCCGACCGTAATTTTTTTGGTGGGGCATTTACCCCGCCACTCGGGCG 359
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 301         AAAATTTTTGCGGTCCGACCGTAATTTTTTTGGTGGGGCATTTACCCCGCCACTCGGGCG 360

Qry 360         ACGTTGGACAAAGCCCTGATCCCTGCACACAAAAACACCAAACCCTCTTGGCGCGCATCA 419
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 361         ACGTTGGACAAAGCCCTGATCCCTGCACACAAAAACACCAAACCCTCTTGGCGCGCATCA 420

Qry 420         TCACGTGGTTCACAACAGACGCTAACCGGTCCAACAATAGGAAGCCGCTGAGCTCGGTAA 479
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 421         TCACGTGGTTCACAACAGACGCTAACCGGTCCAACAATAGGAAGCCGCTGAGCTCGGTAA 480

Qry 480         GGGTTCCTTCAAGTACGCCTGGGTCCTTGACAAGCTCAAGGCCGAGCGTGAGCGTGGTAT 539
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 481         GGGTTCCTTCAAGTACGCCTGGGTCCTTGACAAGCTCAAGGCCGAGCGTGAGCGTGGTAT 540

Qry 540         CACCATCGACATTGCCCTCTGGAAGTTCGAGACTCCCCGCTACTATGTCACCGTCATTGG 599
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 541         CACCATCGACATTGCCCTCTGGAAGTTCGAGACTCCCCGCTACTATGTCACCGTCATTGG 600

Qry 600         TATGTTGCTGTCACCTCTGTCACACATGTCTCACTACTAACAATCAACAGACGCCCCCGG 659
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Ref 601         TATGTTGCTGTCACCTCTGTCACACATGTCTCACTACTAACAATCAACAGACGCCCCCGG 660

Qry 660         CCACCGTG  667
                ||||||||
Ref 661         CCACCGTG  668
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Figure 3: DNA sequencing of the Elongation factor 1-alpha (EF1-alpha) gene.

4. Discussion

Onychomycosis is a fungal infection of nails that may involve any component of the nail unit, including the matrix, bed, or plate. Onychomycosis can cause pain, discomfort, and disfigurement and may produce serious physical and occupational limitations. Fusarium species are common saprophytic non-dermatophyte filamentous fungi that have been frequently reported as etiologic agents of onychomycosis in humans. The most common Fusarium species in human infections are F. solani, F. oxysporum and F. verticillioides [12, 13]. The low incidence of onychomycosis caused by mold (non- Dermatophytes) in some reports, can be for the routine use of cycloheximide in mycological media, which inhibits their growth [14]. In healthy individuals, superficial infection of the eye, skin and nail due to Fusarium are less common [15]. In our study, according to initial clinical signs in a patient, it was suggested that she suffers from melanoma, but mycological examinations (direct microscopy, culture and histopathology) revealed typical septated hyphae branching. The isolated fungus in culture was identified as Fusarium spp in morphological observation. However, for the identification Fusarium species, molecular biology techniques (sequencing) was applied and finally F. solani complex was demonstrated as the causative agent. The clinical form of the patient's nail was distal- lateral subungual and was observed in one nail without extended to other nails. According to the history of the patient, she frequently used lacquer involving and she was in a stressful in period time. In such situations, probably stress was the most predisposing factor for this infection. F. solani is more often isolated from toenails [6, 8] but these data are in accordance with Dordain-Bigot et al which reported the isolation of F. Solani from fingernails [9]. In the current case, the patient was treated with terbinafin initially, but no clinical improve was observed and the relapse of infection was occurring, the treatment was completed by itraconazol pulse therapy (400 mg/day for 8 month). In conclusion, Fusarium species are emerging as a fungus of relevance in medical mycology, since they are less susceptible profiles to antifungal drugs and cause a high mortality rate, especially in immune compromised patients. Early and precise and treatment of this infection requires to early and accurate diagnosis.

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