Case Report
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Down syndrome patient with tinea capitis due to *Aspergillus ochraceus*, the first rare case report

Ahmed Badri Abed[1]*

1 Department of Molecular Biology and Genetics, Faculty of Arts and Sciences, Uşak University, Uşak, Turkey.

Abstract

Introduction: Tinea capitis is a fungal infection of the scalp skin and hair and often caused by dermatophytes. It is the most common type of superficial dermatophytosis in children despite the fact that this infection is not familiar in children with Down syndrome. The infection occurs mainly due to keratinophilic fungi which are anthropophilic and zoophilic species of the genera *Trichophyton, Microsporum and Epidermophyton*, but not by *Aspergillus species* because cutaneous Aspergillosis in general is a rare disease since all types of Aspergillosis infection are more likely to occur in underlying conditions and immunocompromised patients. Limited numbers of published reports referred to scalp mycosis by *Aspergillus species* which were caused by *Aspergillus protuberus* and *Aspergilla niger*. To our knowledge, until so far there is no published report case indicated to *Aspergilla ochraceus* as a causative agent of tinea capitis infection.

Case Report: As well no published report correlated a tinea capitis infection caused by *Aspergilla ochraceus* with Down syndrome child. So we record the first rare case of a typical tinea capitis infection with a rare causative agent which is *Aspergilla ochraceus* in a 6-year-old girl with Down syndrome.

Conclusions: Due to the progressive changing patterns in etiology and clinical manifestation of the diseases caused by *Aspergillus species*, more studies must be perform to include comprehensively all aspects about the pathogenicity of *Aspergillus species* in human especially because of the remarkable increase in prevalence of Aspergillosis during the last few years not only in immunocompromised patients but also in immunucompotent people.

Key words: *Aspergilla spp, Aspergillus ochraceus, Down syndrome, Primary Cutaneous Aspergillosis, Tinea capitis*

***Corresponding Author:** *Ahmed Badri Abed.* Department of Molecular Biology and Genetics, Faculty of Arts and Sciences, Uşak University 64200 Uşak, Turkey**. Phone:** +90 5314236638 **E-mail:** ahmbiq8@gmail.com **Received:** Sep, 2021. **Accepted:** Feb, 2022.

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Introduction

Tinea capitis is a disease refers to the infection of skin and hair of the scalp and is often caused by dermatophytes. Although it is most common in school-age children, it is rarely seen in adults. Animals, contaminated objects and close contact with tinea capitis infected patients are the main cause of infection (1,2). Three genera of keratophilic fungi: *Microsporum, Epidermophyton* and *Trichophyton* are well known to be responsible for these infections (3-6). Although dermatophytes are considered the most responsible cause of cutaneous fungal infections, a non dermatophyte molds and yeast were also found to cause these infections (7,8). From non dermatophytes molds, *Aspergillus species* have been noticed to cause a type of cutaneous infection named as Cutaneous Aspergillosis. Despite the fact that this infection is uncommon opportunistic fungal infection it can present clinically either as a primary or a secondary infection (9). Primary Cutaneous Aspergillosis is uncommon infection and the published reports concerning cases of this infection are rare. The appearance of the disease has been noticed increasingly since the 1970s and this was due to the increase of prevalence of immunocompromised patients. This infection usually occurs in severe debilitating patients this is why the most reported cases were under the category of immunocompromised groups like (malignancies patients, neutropenic hosts, burns cases, tuberculosis, patients undergoing intensive chemotherapy, those who are receiving long-term corticosteroids, antibiotics or cytotoxic drugs, organ transplant recipients and HIV patients (10-12). The most frequent isolated organisms from patients with Cutaneous Aspergillosis are *Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Aspergillus terreus, and Aspergillus ustus* (13, 14). All the former reports about Primary Cutaneous Aspergillosis infection mentioned different cutaneous locations target without referring to the infection of the scalp. But During the last few years, very rare published reports pointed to uncommon *Aspergillus species* that could be a causative agent of a scalp mycosis. These species showed an infection of a typical Primary Cutaneous Aspergillosis. These reports opened the door for a new causative agent to be the main cause of tinea capitis other than common dermatophyes. One of these reports referred to rare cases of tinea capitis in 4 and 9 years children, which were totally different in clinical picture and in etiological aspect which was *Aspergillus niger* (15). Another paper showed a first case of kerion-type scalp mycosis that caused by *Aspergillus protuberus* (16).

Although that tinea capitis is the most common of all cutaneous mycoses in children (17), but it is not a familiar in children with Down syndrome. We couldn't find a published report referred to the infection of tinea capitis in Down syndrome children despite the fact that many survey studies discussed the skin conditions in those patients. These reports revealed that, tinea pedis, tinea corporis and onychocomysis are common dermatophytes infections in people with Down syndrome without mention the scalp infection (18,19). So herein, we present a rare case of 6 years old girl, with Down syndrome who suffered from tinea capitis infection by a totally different etiological agent which considers as a rare causative pathogen until now. The causative fungal pathogen was *Aspergilla ochraceus.* This type of *Aspergillus species* is not a known as a causative agent of any infection of Cutaneuos Aspergillosis, and until now, no other published report referred to any human cutaneuos infection by this species.

Case Report

A 6-year-old female outpatient was referred to our laboratory for diagnosis after consulting with dermatologist due to complaining of severe itching of the scalp, accompanied by hair loss, exudation and crust formation. At the time of examination, it was clear that the child was a Down syndrome patient. During processing of the examination we noticed that the child was with symptoms of (pruritus, hair loss, and erythema) which may suggest of tinea capitis infection. We noticed also that the underlying skin was very erythematous with inflammation and dissemination of the infected area. Samples were collected for microbiological procedures by skin scrapings with scalpel blade. The samples were divided into two parts. From the first part a 10 % potassium hydroxide (KOH) mount was made and direct microscopy was performed. The KOH wet mounts were screened under low power (x10) and then at high power (x40) for visualization of the fungal hyphae, spores and other fungal structures. The second part of the sample was inoculated onto Sabouraud Dextrose Agar and incubated at 25 to 37°C. The cultures were examined every two days. The culture isolates were identified by studying the colony morphology, microscopic examination of the growth.

Laboratory Findings

Microscopic findings

The KOH wet mount which was left for 5-10 minutes and examined carefully revealed strongly the growth of fungi. Different types of fungal shapes were found surrounding the infected hairs. Microscopic examination showed the growth of branched hyphae (Figure 1) and the shaft of the hair was totally filled with small rounded shapes conidial forms with hyphae (Figure 2). After careful examination of the sample, we noticed a rare finding of Hulle cells (Figure 3), which gave a strong diagnostic evidence of an infection with *Aspergillus species*. Microscopic examination pointed to the diagnosis of tinea capitis infection.

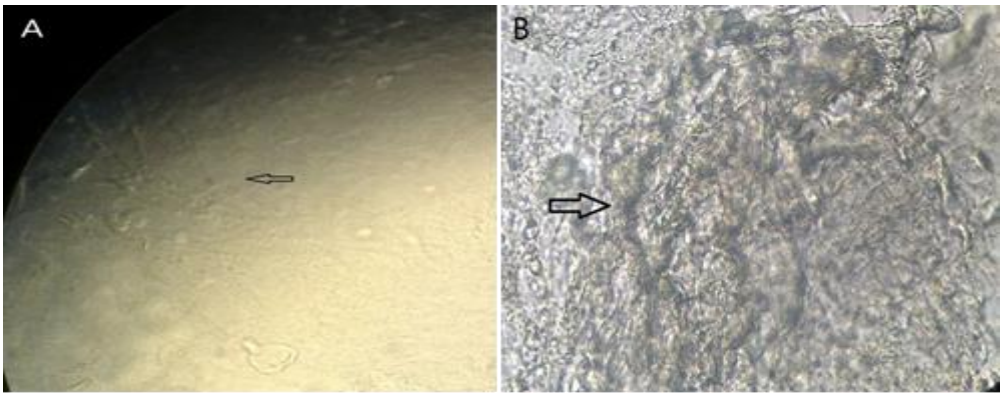

Figure 1. Microscopic examination shows branched hyphae of *Aspergilla ochraceus* (A and B).

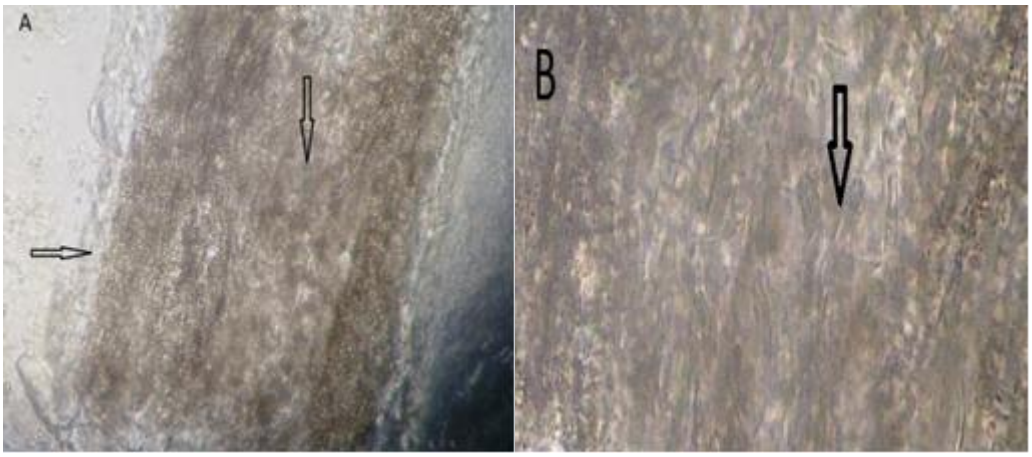

Figure 2. (A) shows the shaft of the hair which is totally filled with small rounded conidial forms with hyphae. (B) The branched hyphae inside the hair shaft.

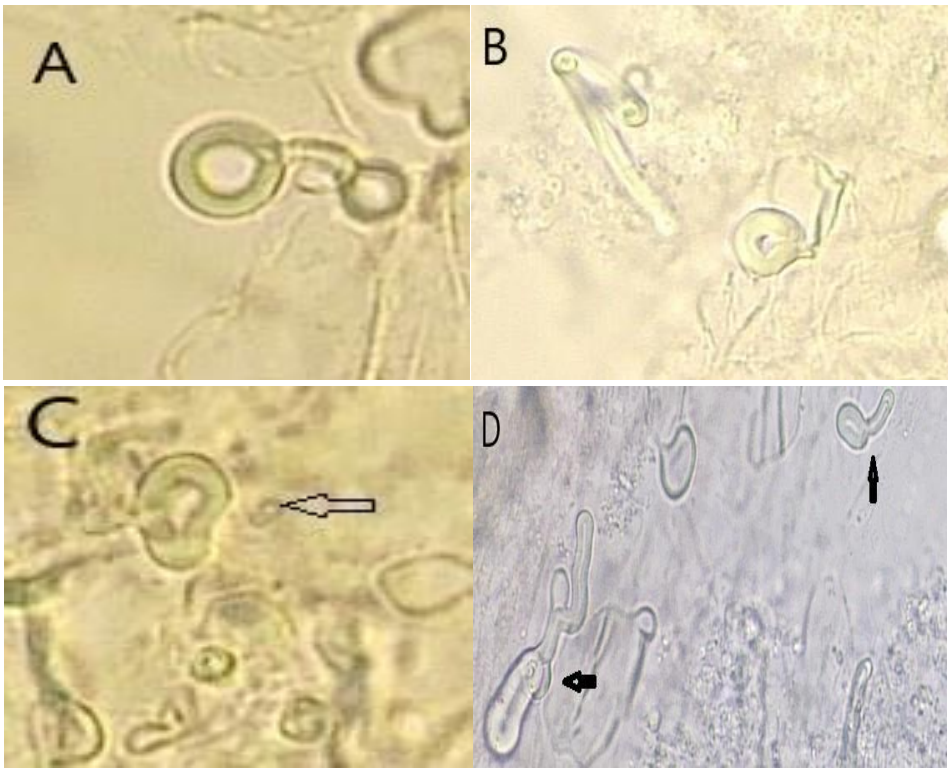

Figure 3. Shows different types of Hulle cells (A, B, C, and D).

Cultural Findings

Colony macroscopic morphology

After Inoculation of the sample onto Sabouraud Dextrose Agar and incubated at 25 to 37°C, an apparent growth was obtained after 5 days on Sabouraud Dextrose Agar plates. The colonies were initially light buff color with rapid spread; eventually, the colonies became mid buff color with a clear white border. Texture of colonies was a woolly to somewhat granular that gives a sandy look and the surface was flat (Figure 4). Colonies gave unremarkable yellowish color on reverse (Figure 5).

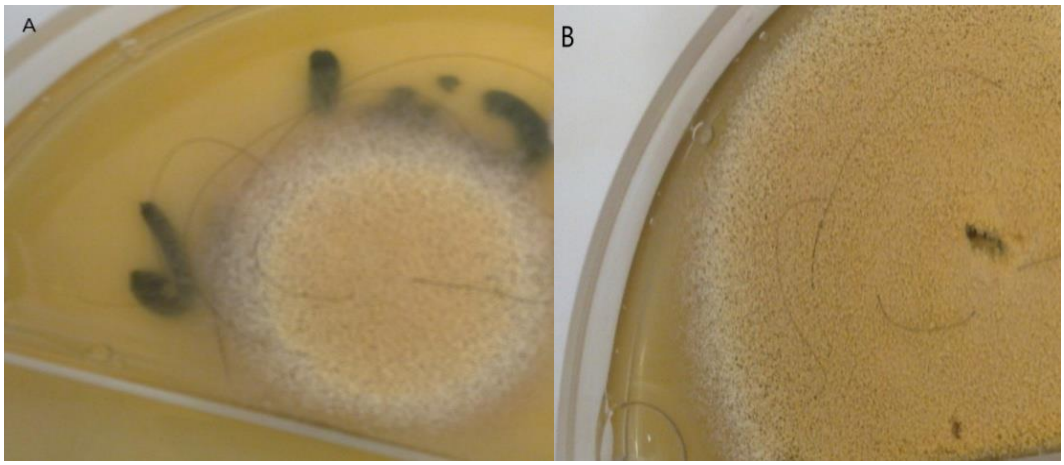

Figure 4. (A) Macroscopic examination of culture shows a light buff color olony of *Aspergillus ochraceus* with a clear white border. (B) Reveals the texture of the colony which is woolly to somewhat granular gives a sandy look with flat surface.

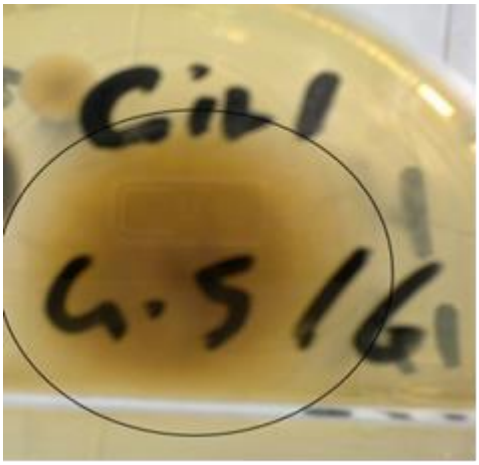

Figure 5. The colony shows Unremarkable yellowish color on reverse.

Colony microscopic morphology

Microscopic examination of the colonies revealed septate and hyaline hyphae. The conidiophores were, thick-walled, dull yellow to light brown, coarsely roughened; vesicles globose, with metulae all over the surface. The conidia were globose to subglobose, delicately roughened, pale green, covering the entire vesicle and pointing out in a radial pattern (Figure 6). The patient has been diagnosed with tinea capitis and the causative fungus has been diagnosed as (*Aspergilla ochraceus)* according to Visagie and Muñoz (20,21).

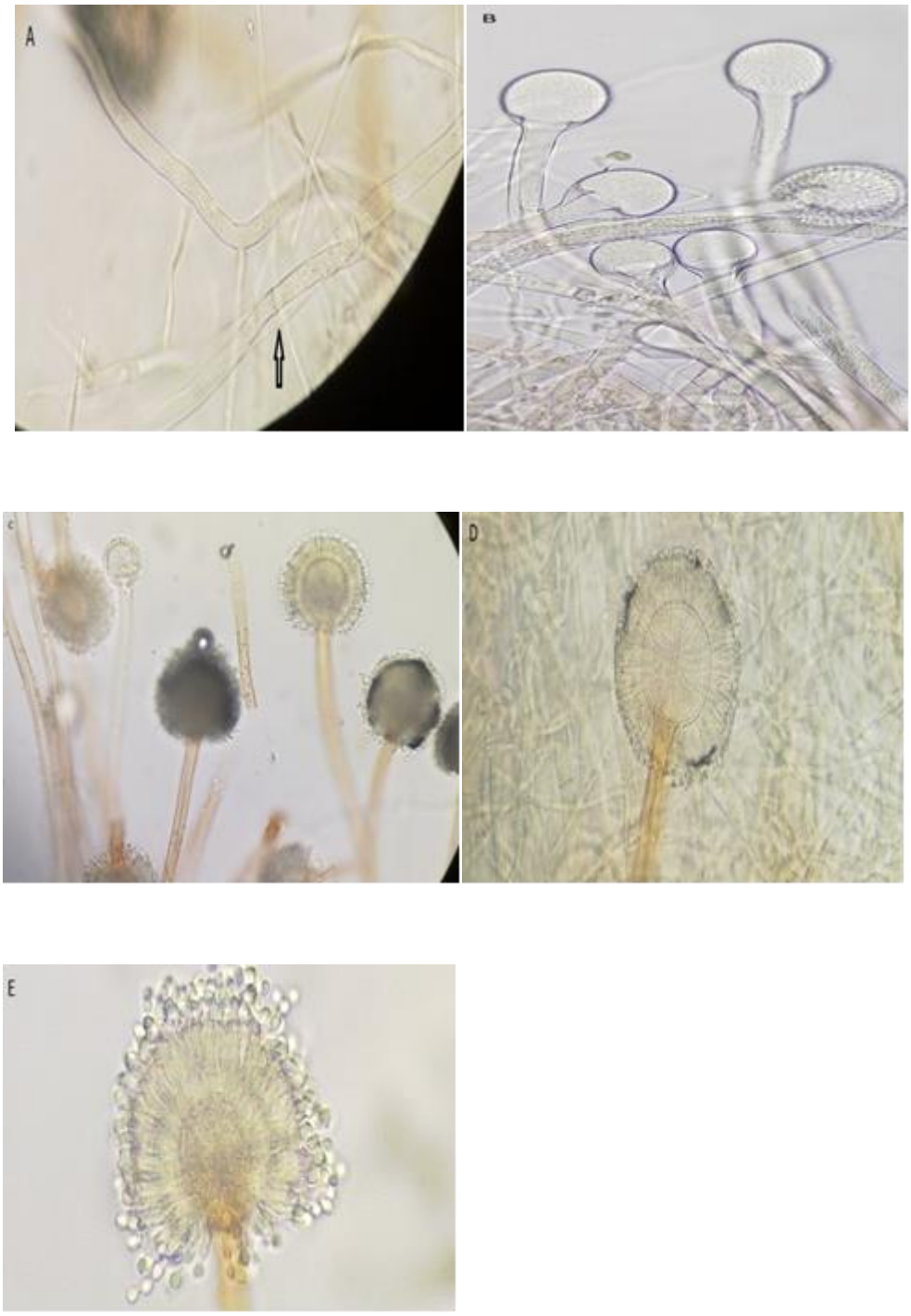

Figure 6. (A) Shows septate and hyaline hyphae. (B) Shows vesicles with globose heads. (C) Conidiophores shapes which look thick-walled, dull yellow to light brown and coarsely roughened. (D) Metulae distributed all over the surface. (E) Conidia are globose to subglobose, delicately roughened, pale green, covering the entire vesicle and pointing out in a radial pattern.

Discussion

Although Primary Cutaneous Aspergillosis has witnessed a significant increase since the 1970s due to the remarkable increase in immunocompromised patients but it still remains as a rare disease (10). With this noticeable increase in cases of Primary Cutaneous Aspergillosis, the types of *Aspergillus species* that found to be responsible of these infections were also noticed to be increased to include (*Aspergillus fumigatus, Aspergillus flavus, Aspergillus niger, Aspergillus terreus, and Aspergillus ustus* (14,22). *Aspergillus species* in immunocompromised patients may infect the lungs, central nervous system, naso-orbital area, and skin in sometimes. The infection may disseminate resulting in high mortality due to severe condition. The rare Cutaneous Aspergillosis infection has been conjugated usually with immune deficiency patients. But the last 20 years has been witnessed an increase in the prevalence of Primary Cutaneous Aspergillosis in immunocompetent patients with a new causative agent of *Aspergillus species* and different locations of infection site (23,24).

In our case the topic is different due to the difference in the immunity status of the patient and also the difference in etiological agent. Down syndrome patient with tinea capitis infection due to *Aspergilla ochraceus* which is a new etiopathogenic agent can be recorded as a first rare published case. Despite the fact that many survey studies investigated the skin condition in Down syndrome patients and fungal infections were found obviously in those patients, we couldn't find the reason behind the rarity of published reports about tinea capititis in children with Down syndrome. One study found a high percentage of fungal infections in those patients and revealed different ratios of infection which were 76.6% for tinea pedis, 8.4% for tinea cruris, and 67.8% for onychomycosis (18). Another study also mentioned two types of infection in Down syndrome patients and the percentage was relatively low comparing with the former findings since the percentage was 4.5% for onychomycosis and 2% for tinea corporis (19).

The incidence of onychomycosis which is a fungal infection of the nail was more than 50% in patients with Down syndrome (18,25). In one survey that included Down syndrome patients, a tinea pedis which is (a fungal infection of the feet) was found in a ratio of 76.6% in those patients. This survey attributed the high incidence of tinea pedis to institutionalization. The study also showed that other dermatophytic infections such as severe onychomycosis and tinea corporis are commonly seen in older Down syndrome patients who are institutionalized (26). Other mucocutaneous study that included 100 children with Down syndrome couldn't isolate any bacterial, fungal or parasitic infestations in those children (27). With all these findings about different types of fungal infection in Down syndrome, we couldn't find observations of tinea capitis in those patients. Regarding the immunity status of Down syndrome patients and if they are immunocompotent or they have some immunodeficiency disorders. A study found some abnormalities of the immune system associated with those patients and these abnormalities included: mild to moderate T and B cell lymphopenia, with marked decrease of naive lymphocytes, impaired mitogen-induced Tcell proliferation, reduced specific antibody responses to immunizations and defects of neutrophil chemotaxis. The study also found a secondary immunodeficiency due to metabolic or nutritional factors, like zinc deficiency. All these factors besides the abnormal anatomical structure of Down syndrome patients may play a role in some infections like respiratory diseases and may

lead to the increased risk of infections (28). Recent findings revealed a significant decrease of B lymphocytes (CD19+) in fetuses with Down syndrome (29). Another study concluded that the immune system is intrinsically deficient in Down syndrome from the very beginning, and besides the abnormalities in thymus and T lymphocyte abnormalities, B lymphocytes are possibly different intrinsically in those patients (30). All these issues can help in understanding the exposure of Down syndrome patients to many infections particularly fungal infections. In our study, the fungal pathogen which was isolated from the scalp of the patient can be considered as a totally different etiopathogenic agent in tinea capitis infection.

Aspergillus ochraceus is a mold in the *Aspergillus* genus and is associated with (ochratoxin A) production a mycotoxin which is known as one of the most food-contaminating agent. It also produces the dihydroisocoumarin mullein and citrinin (31). Bronchopulmonary Aspergillosis and paranasal sinusitis conditions as well the onset and development of asthma in young children have been all associated with *Aspergillus ochraceus* spores (32,33). Furthermore, inhalation or ingestion of (ochratoxin A) found to be seriously and potentially life-threatening with its neurotoxic, carcinogenic and immunosuppresive effects. It can also cause kidney diseases and renal tumors (34). To our knowledge this *Aspergillus species* is not known to cause any kind of Cutaneous Aspergillosis. The only published report which referred to the infection of *Aspergillus ochraceuos* were found in a rare case with calcaneal osteomyelitis in a patient with diabetic foot osteomyelitis (35). The debilitated hosts with (e.g., cancer, burns, and chronic granulomatous diseases) and neutropenia hosts (e.g., patients with leukemia, cytotoxic chemotherapy, corticosteroid therapy, broad-spectrum antibiotic therapy, and human immunodeficiency virus infection) are all at high risk of infection with this fungus (36,37). The probability to get an infection with these fungal species may increase if all other cofactors issues were available, especially that *Aspergillus species* are ubiquitous molds and can be isolated from the soil, air, dust, plants, skin, and nails. Immunological and physical cutaneous barriers constitute the host defense mechanism against *Aspergillus species*. Skin barriers which include keratin and the epidermis give the host a front line of mechanical defense (38). While Macrophages, polymorphonuclear leukocytes and monocytes play together an important role in elimination of this fungus by phagocytize the conidia of *Aspergillus* and damage the fungal hyphae with oxidative and non-oxidative mechanism (39). Some reports attributed chronic or recurrent of dermatophyte infection to disturbance in cell-mediated immunity (40). This is going with the fact that the most common recognizable genetic syndrome associated with immune defects is Down syndrome (41).

Conclusion

We conclude that Down syndrome patients with all these facts about anatomical and immunological defect issues make this category of people as debilitating and predisposing host particularly for Primary Aspergillosis infection. These fungi use the debilitating status of the host to grow and cause the infection. Further studies should be perform in those patients with Down syndrome to investigate the immunity system especially cell mediated immunity which is responsible for fungal infections defense. Also, more survey studies concerning tinea capitis in Down syndrome patients should be available to give more data about this kind of infection which is commonly seen in

children and basically correlated with debilitating issues as a predisposing factor for infection. Due to the progressive changing patterns in etiology and clinical manifestation of the diseases caused by *Aspergillus species*, more studies must be perform to include comprehensively all aspects about the pathogenicity of *Aspergillus species* in human especially because of the remarkable increase in prevalence of Aspergillosis during the last few years not only in immunocompromised patients but also in immunucompotent people.

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