

# Primary cutaneous aspergillosis caused by *Aspergillus terreus* in an immunocompetent woman

Dear Editor,

Aspergillosis is primarily reported in immunocompromised individuals. Primary cutaneous aspergillosis (PCA) caused by *Aspergillus flavus* and *Aspergillus fumigatus* is quite common. Cutaneous *Aspergillus terreus* infections secondary to systemic aspergillosis caused by *Aspergillus terreus* are also familiar. A case of PCA caused by *Aspergillus terreus* characterised by a thick crust on a finger was diagnosed based on histopathology, mycology, culture, and gene sequencing in an immunocompetent woman. It was successfully treated with oral itraconazole and topical terbinafine.

A 64-year-old woman presented with a thick yellow crust on the dorsum of the right index finger for two months, accompanied by occasional mild itching [Figure 1]. The patient stated that there was a red patch on the affected area over the past 2 years and denied any bleeding or preceding trauma. Topical medications were applied on this patch but



**Figure 1:** Primary cutaneous aspergillosis on the dorsum of the right index finger as the thick yellow crust.

gave no relief. She had a history of diabetes but was well-controlled with medication for years.

Histopathological examination revealed epidermal hyperkeratosis, parakeratosis, acanthosis, and localised acantholysis with a small infiltration of eosinophils and neutrophils and active proliferation of basal cells. In the upper dermis, bands of infiltrating lymphocytes, plasma cells, and a small number of eosinophils were observed, along with collagen fibre hyperplasia and small blood vessel proliferation. Periodic acid-Schiff (PAS) staining and fungal fluorescence microscopy revealed hyphae and spores in the stratum corneum, while acid-fast staining was negative [Figure 2a].

Fungal microscopy was positive. The biopsy sample was cultured twice, yielding *Aspergillus* colonies without any growth of mycobacteria [Figure 2b, 2c]. We extracted the partial internal transcribed spacer (ITS) region of the rRNA for gene sequencing and uploaded the result on the national centre for biotechnology information (NCBI) for alignment. It showed 99% homology with *Aspergillus terreus* sequences. Considering its colony morphology and microscopic features, the isolate was confirmed as *Aspergillus terreus*. Drug susceptibility test (DST) performed using the broth microdilution method, Thermo Scientific™ Sensititre™ YeastOne™ (SYO), demonstrated resistance to anidulafungin, micafungin, caspofungin, voriconazole, fluconazole, and amphotericin B, while showing sensitivity to itraconazole, 5-fluorocytosine, and posaconazole.

Routine hematological and biochemical evaluations revealed no abnormal findings. Given the localised lesion and laboratory findings, a diagnosis of PCA was established. The patient was treated with oral itraconazole (200 mg twice daily) for 4 weeks along with topical 1% terbinafine ointment. The lesion showed improvement after 4 weeks of treatment [Figure 3] and completely resolved after 3 months.

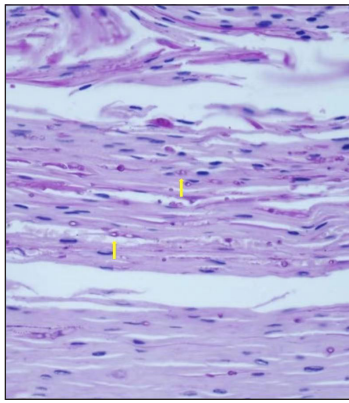
Cutaneous aspergillosis can be categorised into PCA and secondary cutaneous aspergillosis (SCA). The most frequently reported PCA pathogens and their morbidity

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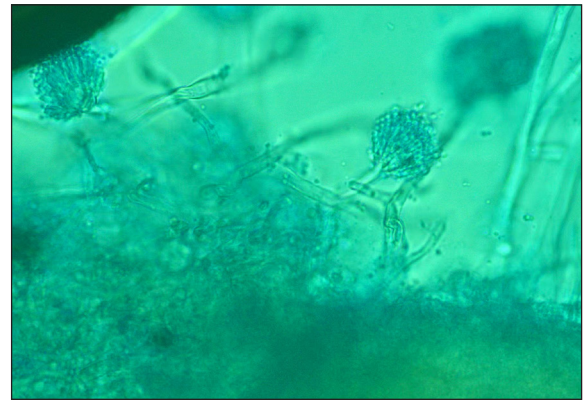
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**Figure 2a:** Hyphae and spores in the stratum corneum, indicated by the yellow arrows (Periodic acid-Schiff staining, 400x)



**Figure 2b:** Culture of *Aspergillus terreus*- cinnamon-brown colonies with velvety texture on Sabouraud dextrose agar



**Figure 2c:** Fluorescent staining of the culture: conidiophores ending in a vesicle covered by phialides bearing conidia (400x).



**Figure 3:** The lesion showing improvement after 4 weeks of treatment.

rates are *Aspergillus fumigatus* (42.3%), *Aspergillus flavus* (35.1%), and *Aspergillus niger* (10.8%).<sup>1</sup> *Aspergillus flavus* appears to be more common in PCA, whereas *Aspergillus fumigatus* is more frequently associated with SCA.<sup>2,3</sup> PCA is usually diagnosed in immunocompetent individuals as well as immunocompromised individuals with conditions such as haematologic malignancy, HIV/AIDS, solid organ transplantation, corticosteroid use, stem cell transplantation, diabetes mellitus, and trauma.<sup>1,4</sup> The clinical presentation of PCA is diverse; lesions usually begin as erythematous, fluctuant nodules and pustules that gradually evolve into crust-covered ulcers.<sup>5</sup> SCA often presents as multiple fulminant maculopapular lesions, typically due to direct or haematogenous spread from an infectious source.<sup>2</sup>

Diagnosis of PCA relies on multiple methods. Histopathological examination using PAS staining is based on the identification

of septate hyphae branching dichotomously at acute angles, which invade the skin. This helps exclude environmental contamination and confirms pathogenicity. However, species identification is challenging based solely on histopathology. Therefore, culture is essential for determining the aetiological agent, given that morphological characteristics vary among different *Aspergillus* species. Gene sequencing further aids in confirming the diagnosis. Since *Aspergillus* is ubiquitous in nature, it is necessary to take primary specimens for repeated cultures to avoid misdiagnosis.

Currently, there are no standard guidelines available for the treatment of PCA. Antifungal therapy combined with surgical debridement may show a lower rate of mortality (13.8%) compared with monotherapy with antifungals (34.6%) or surgery (31.3%).<sup>1</sup> Recurrence rates, dissemination rates, and mortality associated with PCA are reported to be 10.8%, 18.5%, and 31.5% respectively. Diabetes patients tend to have an even higher rate of recurrence (66.7%). However, PCA in immunocompetent individuals generally has a favourable prognosis.<sup>1</sup> For *Aspergillus terreus*, it may be sensitive to itraconazole, voriconazole, posaconazole, isavuconazole, caspofungin, anidulafungin and micafungin, but shows reduced susceptibility to amphotericin B.<sup>6</sup> As an increasing problem in aspergillosis, voriconazole resistance was mostly described in the isolates of *Aspergillus fumigatus*, *Aspergillus flavus*, and cross-resistance between itraconazole, posaconazole, and voriconazole was frequently observed.<sup>7</sup>

In conclusion, the rational use of antifungals guided by drug susceptibility test, continuous monitoring, regular follow-up, and patient education on medication adherence are crucial to prevent recurrence and systemic spread.

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