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Primary Cutaneous Aspergillosis in an Immunocompetent Patient

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A B S T R A C T

Cutaneous involvement in aspergillosis is an uncommon entity. It usually occurs secondary to hematogenous spread from pulmonary infections in immunocompromised patients. Primary infection occurs at site of skin injury following trauma, burn, surgery or intravenous cannulation. As per literature, cutaneous aspergillosis is rarely seen in immunocompetent patients. Common causes reported for cutaneous aspergillosis are A. *fumigatus* and A. *flavus*. Here we report an unusual case of 25 years old immunocompetent male with primary cutaneous aspergillosis. A 25 years old male, presented with multiple ulcers over face including upper and lower eyelid and right cheek. The ulcers were non healing and painful. Initially topical and systemic antibiotics were given but patient did not respond. Then biopsy sample of these ulcers was sent to microbiological lab for bacterial and fungal culture. In KOH mount, thin branched, septate hyphae were seen. In gram staining only pus cells were seen but no bacteria reported. Bacterial culture was negative. Based on these finding antifungal treatment was started. A. *flavus* was identified after one week of fungal culture. Patient responded clinically after antifungal treatment. Cutaneous Aspergillosis although rare entity should be suspected in long standing skin ulcers, which show no response to routine antibacterial treatment. Early diagnosis and antifungal treatment can reduces morbidity and systemic spread in such patients.

Introduction

Cutaneous involvement in aspergillosis is an uncommon entity. It usually occurs secondary to hematogenous spread from pulmonary infections, in immune-compromised patients. Primary infection occurs at site of skin injury following trauma, burn, surgery or intravenous cannulation. As per literature, cutaneous aspergillosis is rarely seen in immunocompetent patients. Common species causing cutaneous aspergillosis are A. *fumigatus* and A. *flavus*. Here we report an unusual case of 25 years old immunocompetent male with primary cutaneous aspergillosis.

Case report

A 25 years old male, who was construction labour by occupation presented with multiple painful ulcers over face for last 6 months. Ulcers started at upper eyelid and subsequently involved lower eyelid and cheek of right side of face. These ulcers were non-healing, erythematous, nodular and painful.

Initially topical and systemic antibiotics were given, in view of bacterial infection for 2 months, but patient did not respond. Despite treatment, ulcers gradually increased in size (3-5×4-7cm). There was no history of any trauma, burn, surgery. He was not taking immunosupressive drugs, neither a known case of diabetes or tuberculosis. There were no other associated medical illnesses and his general health remained good during the entire period of follow up.

A punch biopsy sample from ulcer edge was taken and sent to microbiology lab. In KOH mount, thin(5-9µm width) dicotomously branched, sepatate hyphae were seen. In gram staining pus cells were seen but no bacteria was reported. The biopsy material was inoculated in Sabouraud Dextrose Agar (SDA) with & without antibiotics and incubated at 37°C and 25°C. Bacterial culture was negative after 48 hrs of aerobic incubation. Z-N staining was negative for acid fast bacilli.

H & E stain showed several acute angle branching septate hyphae and giant cells with dense lymphocytic infiltrates.The patient was found to be HIV negative with CD4 count 750cells/mm^3. All other tests, including complete blood counts, Glucose tolerance test, Liver Function Test, Kidney Function Test, HbA_1C were within normal limits.

Based on this finding, antifungal treatment (oral *Itraconazole* 200mg/day) was started. After 4-5 days, wooly yellowish green growth was seen in all SDA slants. In LCB mount from growth, erect conidiophores were seen which terminated in a vesicle covered three fourth with phialides (biseriate).The fungal isolate was confirmed to be *Aspergillus flavus* by the above-mentioned features. Patient showed response within 2 weeks of starting the treatment and lesions completely healed after 8 weeks of treatment.

Results and Discussion

Primary Cutaneous Aspergillosis (PCA) is a rare disease which is mostly seen in immunosuppressed patients. It is extremely rare in immunocompetent patients where it poses a diagnostic challenge (1). Cutaneous aspergillosis can be either primary or secondary, which results from disseminated aspergillosis. Primary cutaneous lesions result from direct inoculation of the *Aspergillus* species from local trauma (intravenous injection site, injury or burns), catheterised patients, contaminated dressings etc. (2).

Fungi of the genus *Aspergillus* are widely distributed in the environment, particularly in soil, water and decomposed vegetation. The most frequent organisms causing cutaneous aspergillosis are *A. flavus* and *A. fumigatus*. Although the patient reported that he had had no history of preceding trauma, we speculate that *A.flavus* was probably inoculated with a piece of wood or soil by doing work at construction site. Primary Cutaneous Aspergillosis may present as erythematous, indurated macules, papules, plaque or hemorrhagic bullae, which may progress to necrotic ulcers that are covered by black eschar. Nodules and pustular lesions although rare, might also occur (3). Our patient presented with multiple ulcers with no immunodeficiency or any comorbidity like diabetes etc.

Treatment for aspergillosis is systemic drug therapy with antifungal drugs like amphotericin B, voriconazole, and Itraconazole. Treatment of primary cutaneous fungal infection is either medical or surgical modalities has been undertaken (4). First-line therapy for such patients was previously intravenous amphotericin B. However, recent studies have suggested that a significant portion of *Aspergillus* species could be resistant to conventional treatment (5).

Voriconazole has been shown to be superior to *amphotericin B*, as a treatment for aspergillosis in adults because of lesser nephrotoxicity but cost is limiting factor. Barret *et al.*, reported the usefulness of topical nystatin combined with systemic *itraconazole* (Fig. 1–3).

Figure.1 Showing no healing ulcers with erythematous nodules

Fig.2 SDA tube showing growth of *Aspergillus flavus*

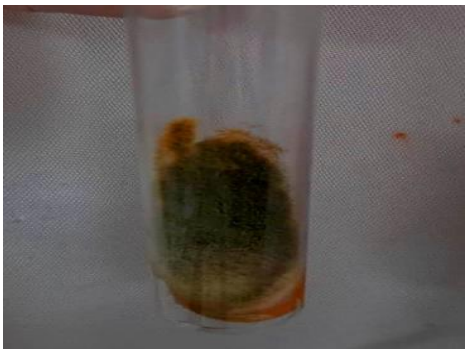
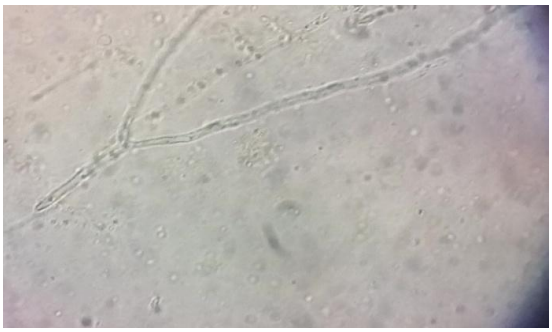


Fig.3 KOH examination showing thin dichotomous septate hypae



In the present case, oral administration of *itraconazole* (200 mg/day) was given because *vericonazole* was not available in hospital and patient was poor .It is therefore important for clinicians to consider the possibility of primary cutaneous aspergillosis, even if the patient is not immunocompromised. (6) Making an early diagnosis of PCA, especially in an immunocompetent patient is a clinical challenge; however, an appropriate treatment

with new antifungal drugs and careful considerations of adjunctive surgical therapy will improve the outcome in such patients.(7)

In conclusion the primary cutaneous Aspergillosis, although rare entity, should be suspected in long standing skin ulcers, which show no response to routine antibacterial treatment. Early diagnosis with a simple KOH examination and antifungal treatment can reduces morbidity and systemic spread in such patients.

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Funding source: No

Ethical approval: Ethical exemption is done by hospital.

Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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