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CASE REPORT

Atypical Nodules in Primary Cutaneous Aspergillosis

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Abstract

Cutaneous aspergillosis is a fungal infection caused by multiple genera of *Aspergillus*. Primary cutaneous Aspergillosis is associated with an immunocompromised state, with prior history of traumatic inoculation. This case report highlights the atypical nodular presentation of Primary cutaneous aspergillosis, contrary to its typical presentation of an ulcer or eschar and its need to be evaluated thoroughly for effective management. Early diagnosis of Primary cutaneous aspergillosis poses a challenge, but a comprehensive approach combining appropriate antifungal therapy with meticulous assessment for adjunctive surgical interventions shows promise in improving patient outcomes. Such an approach not only reduces the risk of systemic spread but also enhances the likelihood of achieving a definitive cure.

Keywords

Subcutaneous fungal infection, Primary cutaneous aspergillosis, Immunocompromised state

Introduction

Cutaneous aspergillosis is a fungal infection caused by various strains within the *Aspergillus* genus, typically presenting in two forms: primary or secondary. Primary Cutaneous Aspergillosis (PCA), less common, primarily affects immunocompromised individuals [1]. It often develops at sites of skin trauma, near intravenous access catheters, under occlusive dressings, or around burns or surgical wounds, facilitating fungal colonization and infection. Secondary lesions may arise from the widespread dissemination of fungal spores through the bloodstream or extension from underlying diseased structures [2]. Early PCA symptoms include erythematous macules with induration, papules, plaques, or bullae containing hemorrhagic fluid. As the disease progresses, lesions may become necrotic ulcers with black eschar, nodules, pustules, or subcutaneous abscesses, indicating increasing severity [1]. In diagnosing cutaneous aspergillosis, histopathological examination (HPE) and culture are crucial. This case report highlights the clinical presentation of multiple cystic swellings on both lower extremities in a patient with multiple comorbidities and an immunocompromised state.

Case Report

A 62-year-old male farmer presented with painless, multiple swellings on both lower extremities and ankles persisting for six months. These initially began as a single lesion following trauma but have since increased in number and size. The patient, who also suffers from Churg-Strauss syndrome, managed with a gradually decreasing Prednisolone regimen, as well as Type 2 Diabetes, Hypertension, and chronic kidney disease, did not report any associated symptoms of pain, redness, discharge, or ulceration.

Upon clinical examination, skin-colored, non-tender, cystic swellings of various sizes were observed, with the largest measuring approximately 4 × 5 cm, predominantly on the lower extremities and smaller ones on the toes. No lymph node enlargement was noted.

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Diagnostic procedures included ultrasound assessment revealing firm masses within the swellings, and fine needle aspiration cytology confirming the presence of fungal hyphae. Biopsy of the cystic swellings showed clear fluid, with negative results on bacterial analysis. Histopathological examination revealed suppurative granulomas with fungal hyphae, notably *Aspergillus flavus*, confirmed by fungal culture (Figure 1, Figure 2 and Figure 3).

Treatment comprised of Itraconazole tablets at 200 mg daily and surgical excision of the affected areas.

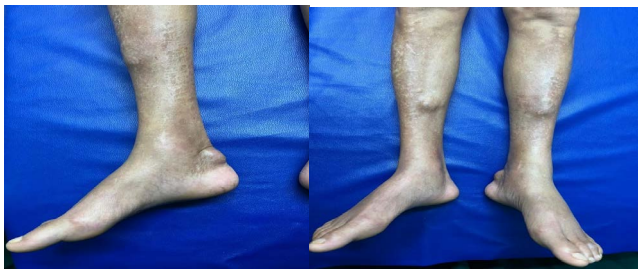

Figure 1: Multiple firms to soft cystic swellings noted over the legs and ankle joint.

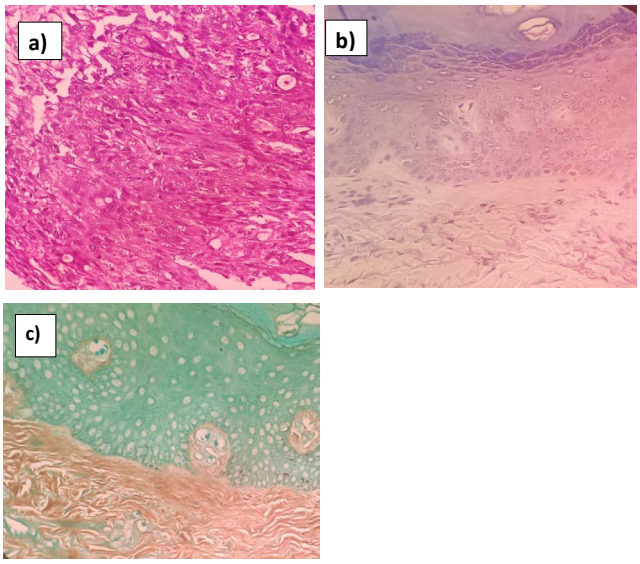

Figure 2: a) Granulomatous inflammation with fungi on H and E staining; b) PAS stain highlights the organism; c) Gomori methenamine stain reveals the fungal spores.

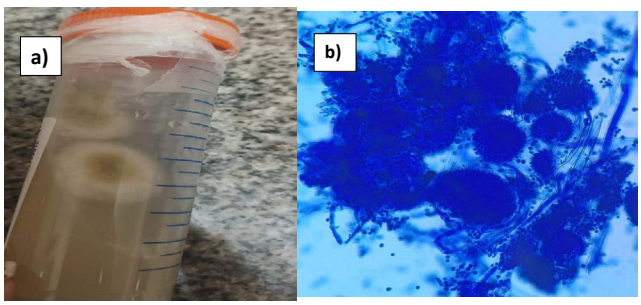

Figure 3: a) *Aspergillus flavus* in Sabaroud dextrose agar; b) *Aspergillus flavus* in Lactophenol blue stain.

Discussion

Aspergillus species encompass a diverse array of saprophytic molds inhabiting soil, air, and plant matter. They are associated with various infections, including superficial and cutaneous mycoses such as distal lateral subungual onychomycosis, proximal subungual onychomycosis, otomycosis, and cutaneous aspergillosis [3,4].

Most skin infections attributed to *Aspergillus* species are acquired nosocomially, with a higher incidence observed among newborns and individuals with compromised immune systems. These infections often occur following surgical procedures, catheter insertions, or as a consequence of occlusive dressings, particularly in patients with burn injuries [5].

The primary risk factors for development of superficial and cutaneous *Aspergillus* infections on the other hand, also include cutaneous trauma and injuries [1].

Additional risk factors contributing to the development of superficial and cutaneous *Aspergillus* infections encompass cutaneous trauma and injuries [4].

Cutaneous aspergillosis typically arises as a manifestation of disseminated *Aspergillus* infection affecting the skin. Initial cutaneous involvement is infrequently encountered. Predominantly, the causative organisms include *Aspergillus fumigatus, Aspergillus flavus, Aspergillus terreus, and Aspergillus ustus* [6].

The prevalence of primary cutaneous aspergillosis remains unclear due to its rarity. According to Patterson, et al., cutaneous involvement was noted in 5% and 4% of cases of invasive aspergillosis, respectively [7]. In patients with this condition, a positive history of traumatic inoculation is often elicited.

Several case reports have documented instances of cutaneous aspergillosis in individuals with compromised immune systems. Nampoory, et al. reported cases of invasive fungal infections in renal transplant recipients, with pulmonary involvement observed in four out of five patients and subcutaneous infection noted in one out of five patients affected by aspergillosis [8].

Prompt diagnosis is crucial for managing cutaneous lesions of primary cutaneous aspergillosis, as they can serve as a gateway for disseminated aspergillosis. This condition is often linked with hematological malignancies and HIV [9].

Primary cutaneous aspergillosis presents with a broad spectrum of manifestations, including erythematous indurated macules, papules, plaques, or hemorrhagic bullae, which serve as the earliest signs. These lesions may evolve into nodules, pustular lesions, necrotic ulcers covered in black eschar, or subcutaneous abscesses [1].

Diagnosis of cutaneous aspergillosis necessitates a skin biopsy. Initially, histopathological examination with hematoxylin and eosin (H & E) is performed to identify septate hyphae with acute angled branching, sporadically fruiting structures, and *Aspergillus* species conidia. Additional confirmation is obtained through specialized fungal stains like Gomori methenamine silver (GMS) and PAS stains [10].

Surgical debridement and antifungal therapy may be used in tandem to treat cutaneous aspergillosis. In certain case reports, oral antifungal medication was sufficient to achieve clearance. Moving to intravenous therapy in the event of resistance to voriconazole or itraconazole. The treatment of PCA with a combination of topical nystatin and systemic itraconazole was successful according to some case reports. Systemic *Aspergillus*-active antifungal medication combined with surgery significantly reduced mortality compared to any other combined or individual method of treatment [9].

The susceptibility of an individual's immune system significantly influences their predisposition to subcutaneous fungal infections, with an observed increase in cases of cutaneous aspergillosis, particularly among immunocompromised individuals.

This case highlights the diverse presentations of primary cutaneous aspergillosis, as it presents with asymptomatic nodules instead of the typical ulceration or eschar formation. It underscores the necessity of considering fungal infections in the evaluation of subcutaneous soft tissue swellings, extending beyond conventional diagnoses like lipomas, fibromas, epidermal cysts, or reactions to foreign bodies.

Early diagnosis of primary cutaneous aspergillosis poses a challenge, but a comprehensive approach combining appropriate antifungal therapy with meticulous assessment for adjunctive surgical interventions shows promise in improving patient outcomes. Such an approach not only reduces the risk of systemic spread but also enhances the likelihood of achieving a definitive cure.

Source(s) of Support

Nil.

Conflict of Interest

Nil.

Declaration of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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