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Primary Cutaneous Aspergillosis in an Immunocompetent Host Presenting as Ulcero-Proliferative Escharotic Lesion

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Abstract: ***We report a case of a 14-year-old immunocompetent male who presented with an extensive ulcero-proliferative lesion with eschar formation on his left thigh. The lesion had evolved insidiously over the course of 1 year, during which excision of the lesion, extended duration wide spectrum antibiotics and even empirical Anti-tuberculous treatment had been administered to the patient, without much benefit. On referral to our centre, the patient underwent biopsy followed by histological examination and fungal culture of the lesion, which turned out to be positive for Aspergillus and was thus diagnosed to be a Case of Primary Cutaneous Invasive Aspergillosis. On thorough investigation there were No signs of any immunocompromised state. The patient was treated with oral voriconazole, daily wound dressing along with nutritional and functional rehabilitation of the patient. Over the course of 12 weeks, there was sloughing off of the eschar and healthy granulation tissue cover at the site of the lesion. This highlights the clinical challenge in the early diagnosis of this rare cutaneous infection, especially in the setting of an immunocompetent host. Institution of appropriate antifungal therapy and local wound care leads to improved outcomes in these patients without the need for surgical intervention.***[1,2]

Keywords: Aspergillosis, cutaneous, eschar, immunocompetent

1. Introduction

Aspergillus is ubiquitous in nature, found commonly in decaying vegetation, grains and soil. As a cause of opportunistic fungal infection in humans, it is next only to Candida species[3]. Usual sites of infection include Lungs, Paranasal sinuses and the Central nervous system. Cutaneous invasive aspergillosis [7, 8], in contrast, occurs relatively less frequently [1], and usually is seen in an immunocompromised host. Cutaneous aspergillosis may be primary, following direct inoculation of the fungus at sites of skin breech such as following trauma, at or near intravenous access catheter sites, and sites associated with occlusive dressings, burns, or surgery. Secondary cutaneous lesions result either from contiguous extension to the skin from adjacent infected organs, particularly the nasal sinuses; or from hematogenous dissemination from a distant infected organ, such as the lungs[4]. Primary cutaneous infection in immunocompetent host is exceedingly rare, and requires a high degree of suspicion for early diagnosis.

2. Case report

A 14-year-old male presented with a large ulcero-proliferative growth on the antero-lateral aspect of the left thigh which had evolved over a period of 12 months. It was a painless nodular, ulcerative lesion at the same site to begin with, which had over the course of one year, evolved to its present size. There was no history of antecedent invasive procedure or trauma to the said site. Prior to referral to our centre, excision of the lesion was attempted, with recurrence, and the patient had received wide spectrum antibiotics failing which an empirical diagnosis of cutaneous tuberculosis was made and anti-tubercular treatment administered for 6 months without any improvement in the condition.

On presentation to us, the patient was vitally stable, of an average built and was poorly nourished with BMI of 18.2. The fungating skin lesion (image 1) measuring 40cm * 25cm had overlying eschar formation with indurated margins. There was no limitation of movements at the hip or knee joints.

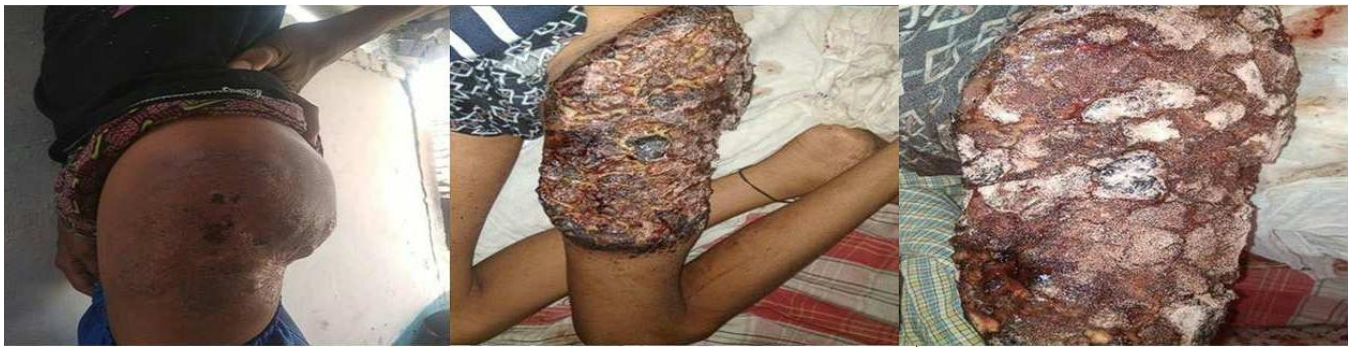

Image 1: Evolution of lesion from nodular ulcerative legion to extensive ulcero-proliferative lesion with eschar formation on antero-lateral aspect of left thigh

Subsequent laboratory investigations showed normal white cell counts with mildly elevated erythrocyte sedimentation rate (31 mm/h). Other routine blood parameters were normal, with the exclusion of Serum Albumin, which was found to be 2.1g/dl. Hepatitis B surface antigen, anti HCV antibody and HIV ELISA were negative. Abdominal Ultrasound, Chest X-ray, Fasting Blood Sugar and Mantoux test were unremarkable.

MRI left thigh was performed (image 2) which showed a heterogeneously enhancing soft tissue lesion along anterolateral aspect of the left thigh, predominantly in cutaneous and subcutaneous plane, with infiltration of tensor fascia lata and gluteus maximus muscle and extension into intermuscular plane of vastus lateralis and biceps femoris muscle, raising concern of a neoplastic etiology. Visualized femur and vessels were normal.

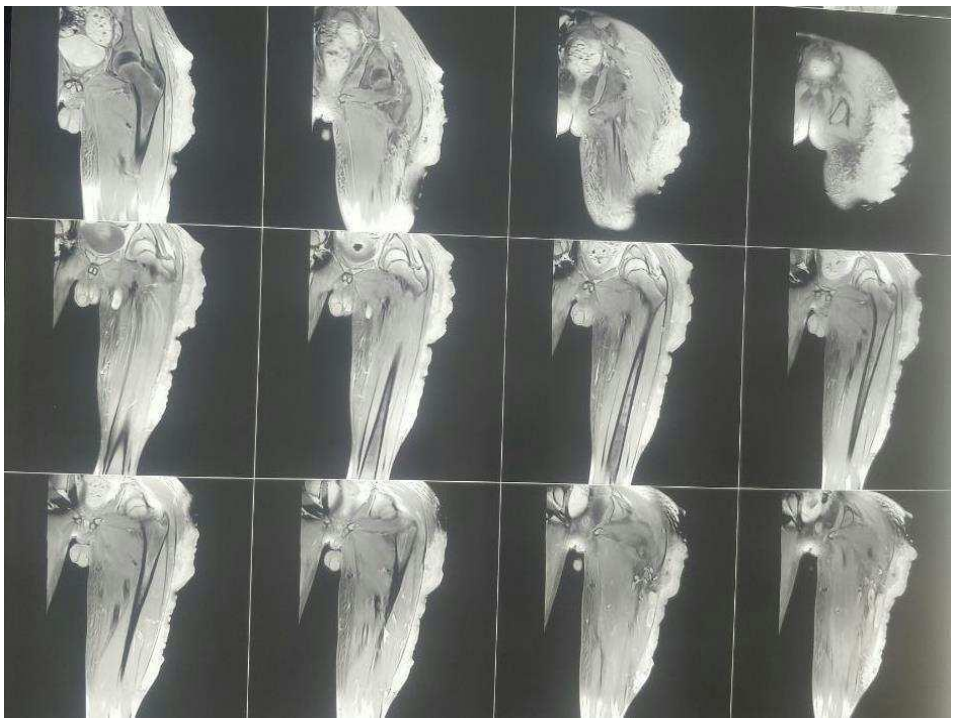

Image 2: MRI of left thigh Demonstrating invasive soft tissue lesion with sparing of neurovascular structures

We performed an image guided biopsy from the core of the lesion as the superficial surface was escharotic and to rule out malignancy by taking representative bites of the tissue. Biopsy results showed a necrotizing granulomatous inflammation, rich in eosinophils with Fungal elements seen on Gomori Trichrome staining. KOH digested direct wet mount revealed few long hyaline septate branching fungal hyphae (Image 3). Subsequent fungal culture demonstrated pure moderate growth of Aspergillus fumigatus.

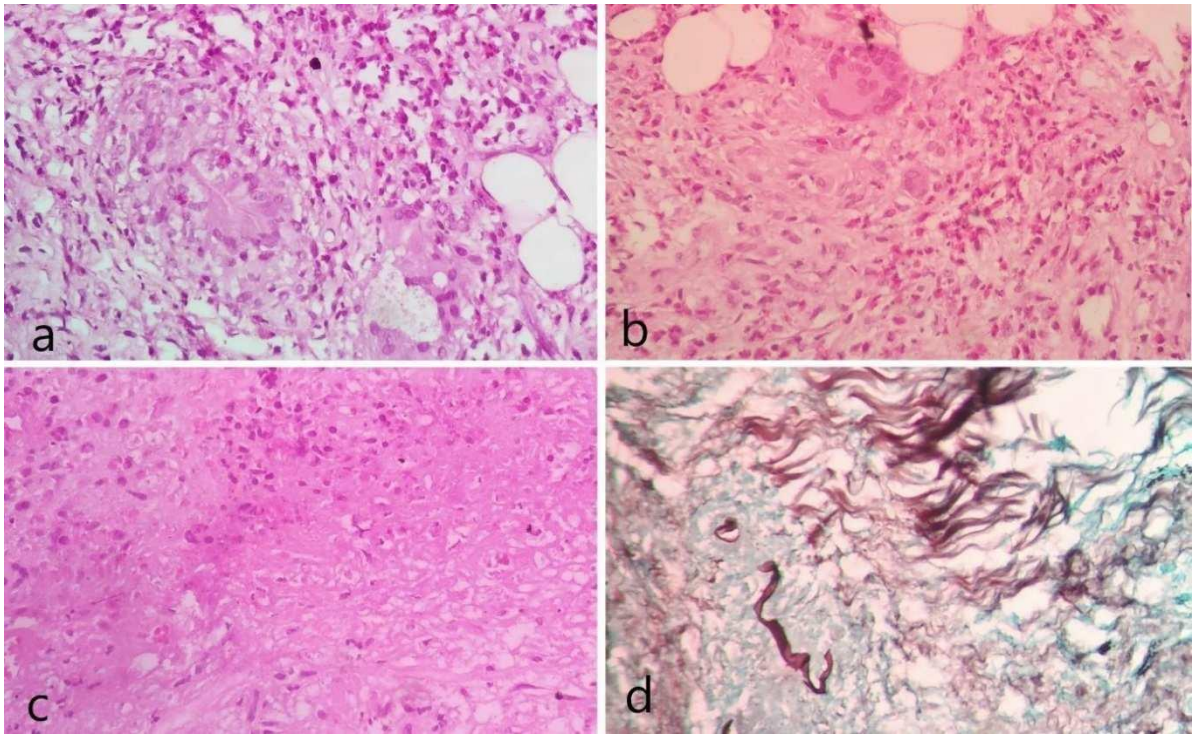

Image 3: (a) Core biopsy showing granulomatous inflammation with Langhans giant cell (H & E X 400) (b) Inflammation rich in eosinophils (H & E x 400) (c) Focus of necrosis (H & E x 400) (d) Gomori trichrome shows fungal hyphae

CT scan of the Chest and the osteo-meatal complex was carried out to look for infection of paranasal sinuses, and was normal. Immunoglobulin and complement levels, along with T and B lymphocyte subset analysis were within normal limits, ruling out any immunocompromised status. Blood and urine cultures were reported as sterile. Sputum bacterial, mycobacterial and fungal cultures showed no growth.

A diagnosis of primary cutaneous invasive aspergillosis was made and the patient was started on oral Voriconazole.

In view of extensive tissue involvement, debridement was not done in this case, as it would have led to further tissue loss and a larger defect. Daily wound dressing was done. Nutritional rehabilitation, limb strengthening exercises in consult with Nutritionist and physiotherapist were carried out. Over a course of 4 weeks, the patient responded well to the treatment and showed gradual improvement in wound state, from the fungating escharotic mass to a well healed granulating wound (Image 4).

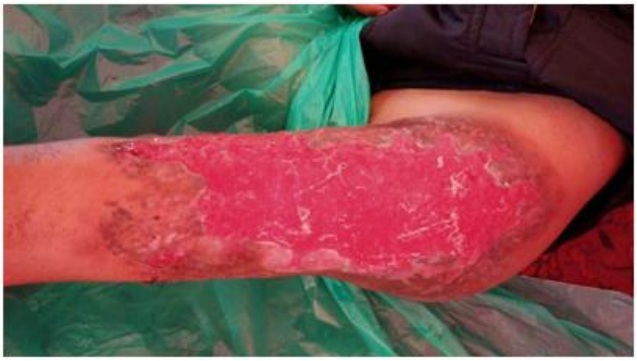

Image 4: Gradual wound healing with sloughing off of eschar followed by healthy granulation tissue cover

After optimal wound healing and nutritional rehabilitation of the patient, he was discharged. Oral voriconazole was continued for 12 weeks during which daily dressings were continued and the wound granulated completely on follow up (Image 5).

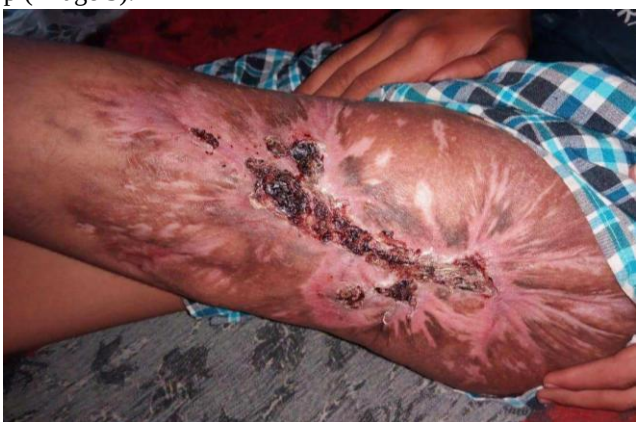

Image 5: Clinical picture at follow up

3. Discussion

Primary Cutaneous Invasive Aspergillosis (PICA) is a rare disease, usually seen in immunosuppressed patients [3]; it is extremely rare in immunocompetent patients and may present a diagnostic dilemma[7]-[8]. Cutaneous aspergillosis may be either a primary infection resulting from inoculation of the fungus at sites of skin breech or secondary to disseminated aspergillosis. Rarely, as in our case, lesions may appear at sites with no apparent antecedent history of skin trauma. Of the many species of Aspergillus, the most common to infect humans is Aspergillus fumigatus. Primary skin infection is usually caused by *Aspergillus flavus*, terreus, niger*and* utus[5].

Indeed, all types of aspergillosis infection are more likely to occur in immunosuppressed patients, patients receiving chemotherapy for acute leukemia or patients receiving corticosteroids [4]. Primary cutaneous aspergillosis can occasionally be seen in healthy patients, as in our case, or can rarely be the presenting sign of underlying immunosuppression, and in the right clinical circumstances this diagnosis should be suspected even if there is no apparent immune defect.

Primary cutaneous aspergillosis can have a variety of clinical manifestations, but the most characteristic lesion is a black eschar that overlies a red or purple patch, plaque, or nodule, usually at the site of skin injury. It may also present as red to purple macules, papules, or nodules with or without overlying erosions or eschars and abscesses. There are no pathognomonic lesions, and hemorrhagic bullae and lesions in a sporotrichoid pattern may also occur[4].

Diagnosis of all types of cutaneous aspergillosis may be made by demonstrating the hyphal forms in the tissue by routine hematoxylin and eosin (H&E) staining; however special stains for fungi such as Periodic acid-Schiff (PAS) and Gomori methenamine-silver (GMS) stains will help to highlight the hyphae[6].

Tissue for these tests should ideally be taken prior to the start of antifungal therapy from the area under and including a necrotic black eschar. Howeverif a black eschar is not present, biopsies may be taken from the most pronounced lesions.

Aspergillus species appear as septate hyphae 3um in diameter that branch at 45 degrees, and can have dermal and epidermal necrosis. Immunocompetent patients may demonstrate a significant granulomatous reaction and few hyphae, as was seen in our case.

Aspergillus species are cultured on Sabouraud dextrose agar; but being a common saprophyte, they may grow as a contaminant in culture. Hence, if obtained in an unexpected clinical scenario, histology with demonstration of hyphae or repeat culture may be advisable.

The differential diagnosis of primary cutaneous aspergillosis includes primary skin infection with other opportunistic fungal organisms such as Candida, Fusarium and Rhizopus species; bacterial infections including staphylococcal or streptococcal abscesses or ecthyma gangrenosum; and typical or atypical mycobacteria. Non-infectious entities which may present like primary cutaneous aspergillosis and are often seen in similar settings of immunocompromise include early Sweet's syndrome and leukemia or lymphoma cutis[7]. In case of a fungating invasive lesion as in our case, soft tissue sarcoma may be considered as a differential in the appropriate setting.

Treatment involves institution of appropriate antifungal pharmacotherapy and adjunctive surgical therapy for wound management on a case to case basis. Systemic Azoles such as Itraconazole or Voriconazole and in more severe cases, Amphotericin B may be used.

Prolonged duration of antifungal therapy over several weeks may be required for complete cure of extensive invasive lesions, such as seen in our case. The decision of debridement or surgical excision versus conservative management of the wound needs to be individualized. Excision without appropriate antifungal cover may lead to early recurrence, as witnessed in our case. Nutritional and Physical Rehabilitation also play a crucial role in optimal patient recovery.

4. Conclusion

Primary Cutaneous Invasive Aspergillosis, is an uncommon infection usually occurring in the setting of an immunocompromised host. However, it may rarely be seen in an immunocompetent host and present a diagnostic dilemma to an unsuspecting healthcare professional. The cutaneous lesion may present with a variable morphology and definitive diagnosis in these cases requires histopathological examination and culture. A combination of systemic antifungal therapy and appropriate wound management will improve the outcome in most patients and while preventing systemic dissemination of infection [5].

Footnotes
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Conflict of Interest: None declared.

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