



## Case Report

## Innocuous “foot lump” in patient with diabetes mellitus: A manifestation of phaeohyphomycosis

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## ABSTRACT

Invasive mycotic infection presenting as “foot lump” in an immunocompetent patient is extremely rare. The case highlights the difficulty in diagnosis of fungal infections of foot including attempts to isolate the fungus and non-response to anti-fungal agents. A 64-year-old lady with T2DM for four years presented with painless, gradually progressive swelling over plantar aspect of left mid-foot for six months. Foot examination revealed soft-to-firm lump over the plantar aspect of left mid-foot obscuring the lateral longitudinal arch. No signs of inflammation or bony deformities were noticed. X-ray foot revealed radio-dense shadow in soft tissue without bone changes, corroborated by MRI. A diagnosis of lipoma, ganglion cyst, tubercular abscess and a fungal infection were considered. Aspirate cytology suggested the presence of *Aspergillus* hyphae although repeated cultures were unsuccessful. Medical management in form of itraconazole initially, followed by voriconazole was tried. However, there was no response to anti fungal agents and the lesion was surgically excised. Histopathological examination confirmed the presence of pigmented fungus (phaeohyphomycosis).

## 1. Introduction

Foot examination is often neglected in patients with diabetes attending busy diabetic clinics, despite an endorsement of annual foot examination and more frequently in case of ‘foot at risk’ by all diabetes professional organizations [1]. An innocuous looking foot lump may be ignored after a cursory examination, unless it is symptomatic or associated with ulcers or significant deformities of the foot. A swelling or lump in foot region may be because of bony deformities after an episode of acute charcot neuroarthropathy because of fracture, collapse of mid-foot or a subcutaneous swelling due to soft tissue abscess, lipoma or a cyst. Foot infections are empirically treated with antibiotics without any prior attempt for tissue culture and microbe characterization [2]. Cutaneous fungal infections presenting as foot lump is uncommon except in developing countries where barefoot walking is common [3], as mycotic infections usually occur as a result of direct inoculation of spores after injury in immuno-compromised patients. Cutaneous mycotic cysts are more commonly attributed to aspergillus species or phaeohyphomycosis. However, primary subcutaneous phaeohyphomycosis in an immunocompetent subject with good glycemic control presenting as lump over sole of foot is not previously reported.

## 2. Case report

A 64-year-old female during routine outpatient visit for diabetes was found to have “lump” over plantar aspect of left mid-foot. On further questioning she revealed that the lump had an insidious onset for 2 years and was associated with dull aching pain and discomfort while walking. She had type 2 diabetes mellitus for 4 years, was on oral anti-hyperglycemic medications, and had no history of bare-foot walking or working in field or garden. She never had foot ulcer or active Charcot’s neuroarthropathy. She had no features suggestive of peripheral sensory neuropathy.

Foot examination revealed a 4 by 4 cm lump at the plantar aspect of left mid-foot with thickening of overlying skin and obscured lateral longitudinal arch (Fig. 1a). The swelling was soft-to-firm in consistency, non-tender, and freely moving over underlying structures suggesting soft-tissue origin. Signs of inflammation, fissures, scar or ulcer were not present. The vibration perception threshold (VPT) was < 10/s, with preserved sensation to Semmes–Weinstein 10-g monofilament and elicitable ankle reflex. All pedal and peripheral pulses were palpable, with ankle-brachial index of 1.1 in either foot. She had no features of diabetic retinopathy on fundus examination. A differential diagnosis of benign soft-tissue tumor of foot including lipoma, ganglion cyst,

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**Fig. 1.** (A) Plantar and lateral view of foot showing soft tissue swelling along the lateral border of mid-foot; (B) x-ray (oblique view) showing a soft tissue homogenous mass with normal bone of the foot; (C) T1-weighted fat saturated (STIR) sagittal MRI images of the left foot showing a soft tissue hyperintense homogenous mass of 4 by 2 cm along the plantar surface and lateral aspect of mid-foot; (D) T2-weighted MRI images of the left foot showing T2-hyperintense homogenous mass along the plantar surface of mid-foot.

sebaceous cyst, plantar fibromatosis; an inclusion cyst, a fungal ball, or abscess (tubercular) was considered.

Investigations revealed hemoglobin 11.4 gm/dl, total leukocyte count (TLC) 8600 cells/mm<sup>3</sup>, erythrocyte sedimentation rate (ESR) 16 mm/h. Her HbA1c was 7.0% and serum creatinine 1.0 mg/dl. Serum galactomannan antigen was not detected (enzyme immunoassay). X-ray of the foot was suggestive of a radio-dense lobulated swelling at the plantar aspect of mid-foot with no bony involvement (Fig. 1b) and chest x-ray was normal. Magnetic resonance imaging (MRI) was suggestive of heterogeneous mass like lesion along the plantar aspect of the foot with no bony involvement (Fig. 1c and d). Tubercular abscess was considered unlikely in view of absence of history of trauma or systemic tuberculosis and normal bone and joints of the foot on radiography. Aspiration of the left foot swelling with a 18 bore needle revealed brownish-yellow color aspirate that was subjected to cytology and microbiological evaluation including bacterial and fungal culture. Cytology of the aspirate revealed predominantly necrosis with few septate fungal hyphae with acute angled branching consistent with aspergillosis. The Ziehl–Neelsen stain for acid-fast bacilli was negative. Repeated attempts to isolate the causative organism were unsuccessful. She was put on oral itraconazole 200 mg twice a day for 12 weeks but with no response and the swelling gradually increased in size. Later, she was initiated on oral voriconazole 200 mg/day.

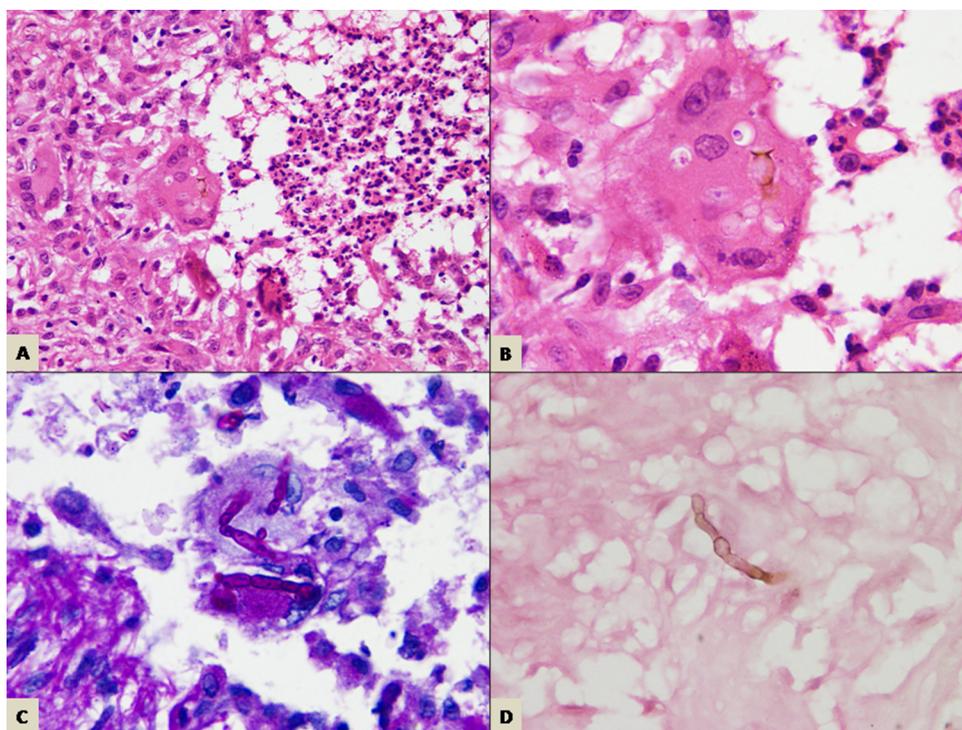
Subsequently, she was lost to follow-up and came after two years with further enlargement of foot lump and worsening discomfort during walking. She underwent surgical excision of the foot swelling. The excision tissue on histopathology revealed a fibrocollagenous cyst wall lined by chronic granulation tissue comprising of foamy histiocytes, lymphocytes, plasma cells and multinucleated giant cells admixed with few neutrophils. Occasional foci of suppurative granuloma and multinucleated giant cells with few hyphal forms of pigmented fungus (phaeohyphomycosis) were identified (Fig. 2a–d). Post-excision the patient is ambulatory, and there is no recurrence of the lump over the past two years. An informed and written consent was obtained from the patient.

### 3. Discussion

Most of the time foot lesions are neglected and referral is not sought because of the absence of ulceration and non-invasive nature of infection. A seemingly innocuous lump over the sole of the foot should not be ignored in a patient with diabetes mellitus, as highlighted in the present case that showed no response to anti-fungals and subsequently requiring surgical excision for the innocuous foot lump that turned out to be phaeohyphomycosis (pigmented fungus).

There are a wide variety of lesions that present as lump of the foot. In the present case, lipoma as the first possibility was considered because of presentation as rather asymptomatic lump over the sole of foot without any signs of inflammation and soft consistency similar to lipomatous lesion of the foot. However, foot especially the sole is an uncommon site for lipoma [4]. MRI is the modality of choice in the assessment of soft tissue tumors of the foot as it suggests a specific diagnosis for certain benign soft tissue tumors of the foot like fat density suggestive of lipoma, presence of cyst wall for ganglion cyst and absence of signs of invasion to distinguish these benign lesions which were considered in the present case including hemangiomas or plantar fibromatosis from malignant tumor [5–7].

Microbiological examination of biopsy material is necessary for identification of the infectious organisms to species level and determining in vitro susceptibility to antifungal agents that assists clinical decision for treatment. Hence, FNAC was contemplated that suggested the presence of *aspergillus* in view of septate hyphae with acute angle branching. However, IDSA guidelines suggest that lack of a positive culture or direct smear result does not rule out the diagnosis of invasive aspergillosis [8]. Therefore, the patient was treated with anti-fungal considering probable invasive aspergillosis, but with no success. Tubercular cold abscess was excluded as tuberculosis presenting as abscess in foot is extremely rare and by the absence of typical granulomas with caseous necrosis on FNA smears and culture specimen; and musculo-skeletal tuberculosis is usually pauci-bacillary and yield negative cultures [9]. The tissue was obtained on multiple occasions for fungal culture but repeated attempts to culture were not successful. The histopathology of the excised lump revealed presence of (brown-colored) pigmented fungal hyphae of phaeohyphomycosis on haematoxylin and



**Fig. 2.** (A) High magnification showing suppurative granuloma with neutrophils-rich center bordered by giant cells containing negative shadows and pigmented hyphal form (haematoxylin and eosin  $\times 400$ ); (B) thick, brown septate pigmented fungus seen within the giant cell (haematoxylin and eosin  $\times 1000$ ); (C) periodic-acid Schiff highlighting thick, septate pigmented fungus within the granuloma (PAS  $\times 400$ ); (D) fungal hyphae highlighted by Masson-Fontana stain due to the melanin pigment within its wall (Masson-Fontana  $\times 400$ ).

eosin stain. Phaeohyphomycetes which includes *Cladosporium*, *Alternaria*, *Bipolaris*, *Rhinochadiella* are black pigmented moulds which are increasingly reported in some groups of patients [10]. It appears as thick, pigmented septate hyphae and is believed to incite a granulomatous host response like any other fungus. The melanin pigment within its wall can be highlighted by Masson-Fontana stain. Rarely, it may be misinterpreted as *Aspergillus* on a preliminary examination; however a careful observation is required for correct interpretation.

*Aspergillus* species are amongst the most ubiquitous fungus, present in water, soil, decaying vegetations and organic debris [8]. Primary aspergillosis usually involves the respiratory tract but other sites may also be involved including bone (osteomyelitis), brain, liver, spleen, lymph nodes (abscess) and skin [8]. Cutaneous aspergillosis may have diverse manifestations including macule, papule, plaque or an ulcer, usually occur in patients on chronic immunosuppressive therapy, post transplant, chronic granulomatous disease etc and are uncommon in immunocompetent person. However, no such predisposing factors for mycotic infection were noted in the present case, as she had good glycemic control and no prior co-morbidities. but presentation as innocuous “foot lump” is not previously reported. Initially a diagnosis of cutaneous aspergillosis was considered on cytology, hence voriconazole was initiated. Medical treatment in form of voriconazole is recommended as primary therapy for most of the patients with cutaneous aspergillosis and surgical resection is indicated in cases of single aspergilloma [11]. The index case did not respond to voriconazole and required surgical excision and histopathology confirmed it to harbor pigmented fungus (phaeohyphomycosis) in the lesion rather than *aspergillus*.

Phaeohyphomycosis have a similar presentation to aspergilloma, as was observed in the present case. Depending on the infection site, phaeohyphomycosis can be classified into a deep systemic, subcutaneous, cutaneous, corneal, or superficial mycosis. Subcutaneous infections occur due to trauma and contamination of wounds by soil, plants, or decomposing wood material, causing direct fungal inoculation. Therefore, phaeohyphomycosis is more common on the extremities, such as the foot, ankle, knees and fingers. Like cutaneous aspergillosis, a cutaneous cyst is the most common presentation of subcutaneous phaeohyphomycosis. On direct microscopy,

phaeohyphomycosis has similar morphology as aspergillus in form of septate hyphae but phaeohyphomycosis is pigmented (black). Histopathology may suggest the presence of suppurative granulomas as seen in the present case. Fungal culture and characterization of mycotic species is needed because of overlapping clinical and FNAC findings amongst these fungal species. The fungal agents implicated for phaeohyphomycosis are *Exophiala*, *Alternaria*, *Bipolaris* and *Xylohypha*, with *Exophiala* as the commonest etiological agent implicated. Surgical excision of subcutaneous phaeohyphomycosis without addition of antifungals is the treatment of choice. However, multi-focal or systemic phaeohyphomycosis will require antifungals like itraconazole, amphotericin-B or flucytosine.

In conclusion, the present case highlights that innocuous looking foot lumps in patients with diabetes require a diligent examination and investigation. It also emphasizes the difficulties encountered in mycotic species characterization and treating fungal infections of foot.

#### Conflict of interest

None.

#### Acknowledgement

None.

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