Fungal infection of the diabetic foot: The often ignored complication

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Citation: Chadwick P (2013) Fungal infection of the diabetic foot: the often ignored complication. *The Diabetic Foot Journal* **16**: 102–7

Article points

1. Fungal infections are generally no more than a nuisance in a healthy population.
2. The development of a fungal infection can contribute to the pathogenesis of ulceration and cellulitis in a diabetic foot in a number of ways.
3. The prevention, identification, and management of fungal foot infection in people with diabetes is important and strategies for prevention should be employed.

Key words

- Fungal infection
- Onychomycosis
- Tinea pedis

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Fungal infections of the foot are a common and uncomplicated occurrence in the general population. However, the consequences of fungal foot infections for people whose peripheral neurological and/or vascular status has been compromised by the sequela of diabetes can be more serious, exposing them to life- and limb-threatening complications. Here, the author reviews the impact of fungal infections on the diabetic foot. Common fungal infections of the foot are briefly described and approaches to prevention, detection, and management among people with diabetes are provided, along with an illustrative case report.

Clinicians are faced with two common appearances of fungal infections of the foot: tinea pedis (athlete's foot) and onychomycosis (nail infection). Within the general population, tinea pedis and onychomycosis both have a prevalence of about 15%–20% and often coexist (Gupta et al, 1998; Thomas, 2010). The most common fungi that cause tinea pedis are *Trichophyton rubrum* (80%) and *Trichophyton interdigitale* (15%), and less commonly *Epidermophyton floccosum* and *Microsporum* (British Infection Association [BIA], 2009).

While fungal infections are generally regarded as no more than a nuisance in the healthy population – itching and discomfort being the most common symptoms (BIA, 2009) – Matricciani and Jones (2012) stress that: "In comparison to otherwise healthy individuals, people with diabetes are at an increased risk of developing fungal infections and are also more likely to face complications, including secondary bacterial infections, foot ulcers, paronychias, cellulitis, osteomyelitis, gangrene, and lower-limb amputation."

The development of a fungal infection can contribute to the pathogenesis of ulceration and cellulitis in a diabetic foot in a number of ways. Interdigital fungal infections can create inflammation and fissuring, leading to breaches in the epidermis. Similarly, in an already dry foot with autonomic dysfunction, tinea pedis can create further risk of fissuring in the plantar arch and calcaneal areas, providing a portal of entry for bacterial infections, which may work synergistically with the tinea pedis to create a deep-seated infection.

The loss of protective sensation associated with diabetic neuropathy may result in patients being unaware of the fungal infection. Equally, if a patient has peripheral arterial disease and vascular insufficiency, this can reduce the tissue viability and protection from damage. The thickening of nails as a result of onychomycosis may cause an increase in subungual pressure and subsequent ulceration, while irregular and thickened nails may cause epidermal breaks as the nails dig into or irritate neighbouring toes, creating ulceration.

Bristow and Spruce (2009) reviewed the relationship between fungal infection of the feet (tinea pedis and onychomycosis) and cellulitis of the low extremities in people with diabetes. Out of a total of 16 studies, they found only two studies that used a prospective case-controlled design with full laboratory tests for the diagnosis of fungal infection.

The first study compared 243 cases of cellulitis with 467 control subjects. Microbiological testing was used to determine the presence of dermatophytes. The infection rate was significantly higher in patients with cellulitis

(56.1%) than in controls (36.4%). Moreover, the results showed that fungal infection of the feet was a significant risk factor for cellulitis, a risk that manifested in interdigital mycoses, onychomycosis, and sole infection.

The second study compared 100 patients with mycosis of the foot with 200 controls. The analysis of fungal cultures demonstrated a positive relationship between dermatophyte infection and cellulitis.

Although people with diabetes are at higher risk of foot ulceration, infection, and lower-limb amputation, this risk level could rise due to the presence of tinea pedis and or onychomycosis (Matricciani and Jones, 2012). This is supported in the literature by studies demonstrating that people with diabetes and fungal nail infection have a higher rate of foot ulceration and gangrene in comparison to people with diabetes without onychomycosis (Doyle et al, 2000; Heald et al, 2001; Mlinaric Missoni et al, 2005; Boyko et al, 2006).

Fungal foot infections

Identification of fungal foot disease is initially based on clinical signs. Fungal nail conditions should be suspected whenever the nail looks abnormal; colour and dystrophy are the most important clues to diagnosis.

Some common presentations include lateral onychomycosis (where white or yellow opaque streaks appear along one side of the nail), distal onycholysis and hyperkeratosis (where scaling occurs under the distal nail, the nail is discoloured, opaque and thickened, and as a result, the end of the nail lifts up), superficial white onychomycosis (where small, flaky white patches and pits appear on the top of the nail plate, the nail becomes rougher and crumbles easily), and total dystrophic onychomycosis (where the nail is completely destroyed). Tinea pedis presents as pruritic, erythematous, and inflamed regions on the foot, commonly between the toes (interdigital), on the sole (vesicular type), or on the medial and lateral aspects (moccasin type) of the foot.

Sampling for fungal infection in the diabetic foot

In the healthy population, there is no need to obtain samples for uncomplicated athlete's foot. However, in an at-risk group – such as people with diabetes – or where oral therapy is being considered, sampling should be undertaken. Swabs are of little value for dermatophytes unless scrapings cannot be obtained (BIA, 2009). Skin should be scraped from the advancing edge of the lesion and skin flakes greater than 5 mm^2 are needed for microscopy (BIA, 2009).

Nail samples should be taken from the most proximal edge of the diseased nail as this is where most viable fungi are found. The clippings should be full thickness (BIA, 2009). If the advancing edge is too deep to cut back, drilling a hole in the nail and curetting it out can yield better results (Sumikawa et al, 2007).

Management of fungal infections of the diabetic foot

The prevention, identification, and management of fungal foot infections in people with diabetes are important. To prevent the development of fungal infections, Matricciani and Jones (2012) suggest maintaining good foot hygiene and treating any mild tinea pedis before infection spreads, as well as wearing well-fitting shoes (without high heels or narrow toes). Shoes should also be kept dry, which can be achieved by alternating shoes on a daily basis.

Old shoes that may have become colonised should be replaced. Clean, absorbent socks are recommended, preferably made from natural fibres, such as cotton. When in communal areas, the individual should avoid direct contact with the floor by wearing flip flops and never wear other people's shoes. The optimisation of blood sugar levels should also be encouraged.

Treatment

Most studies into the treatment of fungal infections involve healthy individuals. The recommendations of the BIA (2009) for such individuals are: dermatophyte infection of the skin – terbinafine is recommended as it is fungicidal (kills fungus), as opposed to fungistatic (prevents fungal development). The BIA (2009) recommends a 1-week course of topical 1% terbinafine applied once or twice daily. If the infection is intractable, the BIA (2009) recommends the consideration of oral terbinafine for 4–6 weeks.

If a dermatophyte infection of the nail is present, the BIA recommends the use of oral

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terbinafine (250 mg once a day for 3–6 months; Crawford 2006; 2007; Hunt, 2008). For a nail infection with non-dermatophyte moulds (such as *Aspergillus* sp. or *Candida*), oral itraconazole (which is a pulsed therapy – three courses of 7 days/month) is recommended (BIA, 2009). These BIA recommendations cannot necessarily be extrapolated to people with diabetes.

Considerations for infection management in the person with diabetes

People with diabetes should follow the guidelines described for the general population. However, Tan (2004) suggests that people with diabetes tend to be more resistant to treatment with traditional antifungal regimens due to hyperglycaemia and difficulty in maintaining good foot hygiene (usually due to neuropathy, obesity, or retinopathy).

The second major issue is the role of polypharmacy. Grant et al (2003) identified that many people with diabetes experience polypharmacy. Increasing an already large pill burden – and the risk of drug interactions – must be considered (British National Formulary, 2013). There are many other potential interactions that must be considered when prescribing oral therapies for the treatment of fungal infections.

Case study

A 67-year-old man with type 2 diabetes (HbA_{1c}, 8.3% [67 mmol/mol]) had a history of ulceration following a total nail avulsion. Ulceration had occurred between the first and second toes. Swabs were sent for culture and sensitivity, and they grew *Staphylococcus aureus*, which was sensitive to the flucloxacillin. This developed into cellulitis, which was treated with dressings and a 2-week course of flucloxacillin (500 mg, four times a day).

The foot settled and the patient was referred back to the preventative foot care programme with emergency access advice. He was advised to use a daily emollient on the dry dorsal area, but to avoid moisturising the interdigital spaces to prevent excessive moisture.

The patient presented 2 weeks later as an emergency with spreading cellulitis (*Figure 1*).

It was suggested that the individual may have experienced an adverse reaction to the emollient, or a renewed bacterial infection. Flucloxacillin therapy was restarted and swabs were taken for culture and sensitivity. Skin scrapings were also sent. The clinical impression was of a synergistic bacterial and *Candida* infection. In conjunction with the flucloxacillin, the patient was also commenced on fluconazole (100 mg, once a day). Swabs and skin scraping results confirmed the clinical diagnosis.

After 2 weeks, the foot had improved significantly (*Figure 2*) and flucloxacillin was discontinued. Due to ongoing interdigital irritation, it was decided to continue the fluconazole for a further 2 weeks.

Conclusion

Fungal infections of the foot in people with diabetes should not be ignored. They potentially have a role

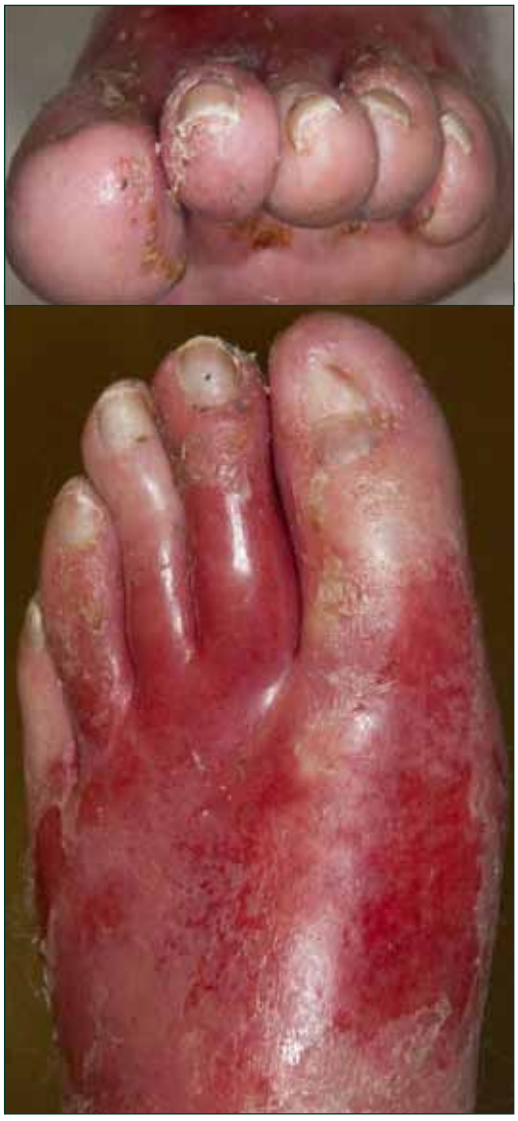

Figure 1. Two views of the patient's foot at presentation. Note the spreading cellulitis.

in the pathogenesis of ulceration; the literature suggests a high risk of secondary bacterial infection. Treatment should be initiated early to prevent spread, and preventative measures should be used to avoid infection and re-infection. Treatment must involve careful consideration of the person's comorbidities and other medications. ■

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Figure 2. The patient's foot 2 weeks following presentation.