ONYCHOMYCOSIS IN DIABETES

Complications of the feet are a major cause of morbidity, mortality, and disability in persons with diabetes. A relatively common disorder, diabetes mellitus affects over 16 million people in the United States. The World Health Organization predicts that by the year 2010 the world’s diabetic population will double to over 200 million people. Diabetes affects persons of all ages and in all socioeconomic segments of the population. There are over 625,000 newly diagnosed diabetics entering the health care system in the United States each year. Nontraumatic lower extremity (LE) ulcers and amputations associated with diabetes are an important and costly problem. Because of the morbidity and complexities of the disease, total direct health care costs spent for patients with diabetes are higher than for those in the general population. In the United States, patients with diabetes use health care resources at a rate 3 times higher than patients in the nondiabetic population. The average number of outpatient visits made to health care providers each year is 15.5 per patient with diabetes compared with 5.5 per patient in the general population. In addition to these direct costs, society faces indirect costs relating to diabetic complications that result in loss of productivity.

Diabetes is the most common reason for nontraumatic LE amputations in the United States. In 1985, more than 50,000 LE amputations were performed on persons with diabetes. Epidemiologic data suggest that in individuals with diabetes, foot ulcers preceded 85% of amputations. This places an enormous burden on the health care system. In addition, the 5-year mortality rate after LE amputations among the diabetic population is reported to be as high as 68%.

PREVALENCE OF ONYCHOMYCOSIS IN THE DIABETIC POPULATION

Onychomycosis is the most common nail disorder, probably representing about 30% of cutaneous fungal infections. Gupta and colleagues investigated the prevalence of onychomycosis in 550 patients with diabetes. They found clinically abnormal nails in 46% of patients and mycologic evidence of dermatophyte infection in 26% of patients. The presence of onychomycosis was correlated with age and with male gender. In fact, males with diabetes were 2.99 times more likely to have onychomycosis than females with diabetes. The overall risk ratio of individuals with diabetes having onychomycosis is 2.77 compared with age- and sex-matched nondiabetic controls.

ONYCHOMYCOSIS AND FOOT PROBLEMS IN DIABETES

Diabetes mellitus causes complications in a number of organ systems, including the renal, ocular, cardiovascular, neurologic, and cutaneous systems. The diabetic foot is a complex condition that has many features, including neuropathy, impaired wound healing, immune compromise, peripheral vascular disease, and trauma and infection. The cutaneous problems of the LE in individuals with diabetes are generally related to peripheral vascular disease, diabetic neuropathy, and trauma.

There are no studies that investigate onychomycosis and tinea pedis as potential risks for diabetic foot ulcers. Although mild, early onychomycosis probably poses little danger to a person with diabetes; more severe and neglected onychomycosis can present a threat. In particular, the high-risk person with diabetes (defined as a person with type I or type II diabetes who has sensory neuropathy and impaired circulation of the LE) may be at increased risk of experiencing complications from onychomycosis. Onychomycosis results in thick, yellow brittle nails that can be sharp and pointed, causing injury to the surrounding skin. The diabetic individual with neuropathy does not notice small cuts and breaks in the skin, which can become a portal of entry for bacteria. When ignored, these minor infections can escalate into serious paronychia and cellulitis (Fig 1). Just as tight shoes can cause a friction blister in
the neuropathic diabetic patient, thickened, dystrophic mycotic nails can cause pressure erosions of the nail bed and hyponychium. These skin breaks, unnoticed by the patient because of sensory neuropathy, can result in serious limb-threatening bacterial infections (Figs 2, 3, and 4). Because of the close proximity of the nail bed to the underlying bone, osteomyelitis can result from neglected, infected nail bed erosion in the person with diabetes.

The lack of long-term outcome studies makes it impossible to determine how many diabetic patients have potentially preventable bad outcomes as a result of untreated onychomycosis. Amputations of the LE are a common cause of morbidity in the diabetic population and a large expense to society.

TINEA PEDIS IN DIABETES
A study of 32 patients with diabetes and onychomycosis noted that two thirds of the patients had coexisting dermatophyte skin eruptions, most commonly tinea pedis. Neglected acute and chronic tinea pedis can become a problem for persons with diabetes. Because of the LE compromise seen in high-risk diabetes, tinea pedis presents a significant concern. Interdigital web-space tinea pedis may lead to cracks and fissures. These can become secondarily infected, resulting in serious deep space infection (Fig 4).

MANAGING ONYCHOMYCOSIS AND TINEA PEDIS IN DIABETES
Treatment of toenail onychomycosis in the high-risk diabetic patient requires a 3-pronged approach that involves oral antifungal therapy, mechanical/physical measures, and patient education (Table I).

Antifungal therapy
The cornerstone of the management of fungal skin and nail disease in diabetes is oral antifungal

Fig 1. Paronychia from ingrown mycotic nail in diabetic patient.

Fig 2. Neurotrophic ulceration in type II diabetic.

Fig 3. Neurotrophic ulceration in type II diabetic.

Fig 4. Nail bed ulceration in neuropathic type I diabetic.
therapy. It is the author’s opinion that the nails and skin of high-risk patients with diabetes should be cleared and maintained free of fungus indefinitely. In selecting an oral antifungal medication for such patients, the clinician should consider efficacy, compliance, concomitant medications, and cost.

It should also be noted that relapse or reinfec-
tion is seen in this population, perhaps because of impaired LE circulation, slow growth of nails, and immunopathy. Although there is no supportive research evidence, it is generally believed that topi-
cal antifungal drugs are useful in the prevention of relapse and reinfection of fungal skin and nail disease.

Both terbinafine and itraconazole have been evaluated in diabetics and found to be safe. In 32 patients with onychomycosis, oral terbinafine 250 mg daily for 12 weeks with a 60-week follow up resulted in a 61% complete cure rate and an 89% mycologic cure—results as good as those for normal hosts. Concomitant tinea pedis cleared in 95.2% of patients at week 72. Over half of the patients were taking oral antidiabetic drugs and there were no drug-drug interactions reported.7 In a study of diab-
etics with onychomycosis and LE compromise treated with intermittent itraconazole 200 mg twice daily, 4 of 27 patients experienced mild side effects.8

Table I. Treatment of onychomycosis in the high-

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<th>Risk* diabetic patient</th>
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<td>Oral antifungal therapy</td>
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<td>Physical debridement; clipping and grinding of sharp, pointed, thickened mycotic nails</td>
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| Patient education about the importance of proper foot self-examination and care; also includes routine treat-
ment with topical antifungal therapy to clear and prevent recurrences of tinea pedis |

*Person with diabetes (type I or type II) who has sensory neuropathy and impaired circulation of the lower extremity.

Mechanical intervention

Physical debridement of the fungal nail by manu-
al or electric means is an important part of the manage-
ment of diabetic feet and toenails. Avulsion is rarely indicated, but there may be a need for grading and debridement of sharp thick nails that are otherwise difficult to manage and risky to ignore. An electric file or grinder is used to reduce thickened fungal nails. A mask should be worn to avoid inha-
lting the nail dust and fungal particles.

Patient education

The high-risk patient with diabetes should be educated about the importance of proper foot care and should be instructed to examine his or her feet and toenails daily. Self-examination should include careful inspection of the web spaces, heels, and peri-
omicintum to determine whether there are small cuts and breaks in the skin. Although these small cuts may seem insignificant, they can lead to serious problems if left untreated. The patient should be reminded that he or she cannot rely on pain and dis-
comfort to signal breaks in the skin, because diabet-
ic neuropathy often impairs sensation. It is beneficial to use each office visit as an opportunity to examine the feet and nails and talk to the patient about the importance of general foot care and prevention of fungal disease. By examining the feet and nails of every diabetic patient seen in the office, regardless of the patient’s chief complaint, the physician emphasizes the importance of the health and condition of the patient’s feet and toenails.

SUMMARY

Severe LE bacterial infection with resultant ampu-
tation in persons with diabetes is costly both in terms of health care use and loss of productivity from morbidity, mortality, and disability. Although there are no long-term prospective studies that prove onychomycosis treatment prevents serious sequela, common sense suggests that preserving the cutaneous integrity of the LE is useful for the compromised patient with diabetes. A recent study shows that oral agents such as terbinafine can effect-
tively treat and cure onychomycosis and concomi-
tant skin infection (dermatophytosis) in patients with diabetes.7 The cost savings from prevention of LE complications is significant, making the expense and effort needed to treat onychomycosis and tinea pedis in patients with diabetes a sound investment. LE amputation in individuals with diabetes is the pri-
mary cause of disability and death in this population. Education of such patients about the importance of foot and nail care is paramount.

REFERENCES


DISCUSSION

Dr. Jorizzo: I would like to comment on my treatment approach and on my experience with recurrence. When terbinafine was first approved, I started using it in all patients who had severe disease, including patients with diabetes. I found that I was getting a few early recurrences. Most of the available data is on later recurrences. I think there is a correlation between recurrence and the fungicidal effect of the agent.

We have been involved with clinical trials for both terbinafine and itraconazole. Inclusion in these trials required the patients to have several millimeters of normal nail. We had to exclude patients who had nail disease all the way down under the cuticle. In the real world, however, and especially in the diabetic population, I have found that most patients have full nail dystrophy. My empirical opinion is that patients with full nail dystrophy, especially in coexisting diabetes, need 4 months of therapy. I would like to see data, but what I have been doing subjectively is saying up front to those patients, “Look, we don’t have data on your kind of nail involvement. We have data on only infections involving a couple of millimeters of normal nail, so I’m going to recommend 4 months of treatment.” I feel, anecdotally, that this duration has been effective with patients with diabetes. And because I believe they have a cellular immune “blind spot,” I put all my diabetic patients on prophylactic therapy when they finish their course.

Dr. Wolf: How do you do that?

Dr. Jorizzo: There are a number of ways to do that. I usually recommend miconazole nitrate 2% powder. I think because the recurrences appear later, the mechanism is to get it in the toe web and into the nail. So I have it applied in the toe webs every third day or so. Obviously we need data on this, but it makes sense to me.

Dr. Pollak: In my estimation, if there is a need for oral antifungals in the treatment of onychomycosis, it certainly is with the diabetic population. If a managed care organization is trying to decide who is going to get one of the newer oral antifungals, it certainly should be patients with diabetes, because we do see serious complications with these patients.

I would also like to make a clinical note. If an ulcer occurs on a digit, whether it be from a long fungal toenail digging into that toe or a nail bed being ulcerated, I believe x-rays are not good diagnostic tools for osteomyelitis in one’s toe. On the other hand, a bone scan can be deceivingly sensitive. If a bone scan is performed on a patient who previously underwent a phenol and alcohol nail procedure from a podiatrist, the area will show up “hot” on the scan. I have seen patients lose a toe because of an inflammatory response to the phenol. They saw another doctor because the toe was not healing quickly enough, they had a hot bone scan, and they had the toe amputated.

When trying to determine whether there is osteomyelitis on a digit that is chronically swollen and draining, examine the depth of the ulcer (the deeper it is, the more likely it is osteomyelitis). If you can see exposed bone when probing with a sterile swab, most likely it is osteomyelitis. At that point I would consider amputation, but this can be a clinically difficult evaluation for many practitioners, depending upon the doctor’s orientation.

Dr. Wolf: Is it important to treat tinea pedis in the diabetic patient?

Dr. Rich: It think it is very important to treat, clear, and prevent tinea pedis in the patient with diabetes. We have all seen cases of fissures in web spaces and also in moccasin-type tinea pedis around the heel.

Dr. Wolf: So you recommend treating it initially and then making prophylaxis an important part of the approach?

Dr. Rich: Yes, and sometimes treating it orally initially. I think a case can be made for 1 month of an oral antifungal drug.

Dr. Fivenson: I run a large wound care clinic, and I think it is actually more important to treat interdigital and moccasin-type tinea pedis than the nails in the diabetic patient, because these are problems that are going to predispose the patient to fissures and ulcers. I think we need to emphasize in any kind of standardized format how important it is to hydrate those feet with emollients to prevent fissures. Dry skin in diabetes is a perennial problem, especially in the feet.

Furthermore, off-loading must be more specifically emphasized as a complete management package for diabetic foot. If you have onychomycosis but are not bearing weight on that toe, it will heal. It is the
continuous cramming of the toes into tight shoes that is the problem. I, too, use prophylactic treatment right after complete or incomplete treatment because of the essentially nonexistent growth rate of the nails. I recommend a topical antifungal for prophylaxis, either a powder (we frequently use miconazole nitrate) or a once-weekly chronic course of a topical azole to prevent reinfection. The onychomycosis is less important than the tinea pedis because of the reservoir that creates a situation where you have macerations that other pathogens can enter.

Dr. Scher: Is the use of miconazole nitrate better than a topical antifungal cream?

Dr. Fivenson: My gut impression is no. I think the key thing is that these patients are doing something about their feet. They have to look at the feet, because they cannot feel them, when they apply the powder or cream. Powder is easier, because they can also sprinkle it in their shoes.

Dr. Pandya: We know that it takes about 7 days to reach minimal inhibitory concentrations (MICs) of oral antifungals in the nails, because those drugs absorb through the nail bed. Then once you stop the drug, it stays active for 84 or 90 days afterward. I wonder about the microangiopathy in the person with diabetes in terms of delivery of drug to the matrix and to the nail bed, regardless of whether you have taken nail clippings. Do you know whether there are any studies that have looked at patients with diabetes to see whether it takes longer than 7 days to reach the MICs in the nails and whether it is fewer than 84 or 90 days that the drug stays above the MIC?

Dr. Rich: I do not know of any studies that have looked at how the patient’s angioopathy affects MICs and how long the drug remains active in the system.

Dr. Atillasoy: A study that has not yet been published (by Phoebe Rich, et al) evaluated 32 diabetic patients who were treated with terbinafaine for onychomycosis, which they had for a mean of 20 years. Twenty-one of the patients also had tinea pedis or tinea corporis. At least 20 of these 21 patients (95%) had fully cleared skin infection (clinically and mycologically), and they stayed clear at week 72 with no relapses in the skin. For tinea pedis, the mycologic cure rate was 89% and the complete cure rate was 61%.

Dr. Jorizzo: Did the onychomycosis include the entire nail, or just several millimeters of the nail?

Dr. Atillasoy: The study did not exclude total dystrophic onychomycosis.

Dr. Smith: When we get into prevention, though, aren’t we really working without any data at all and then don’t we fall back on what we think represents our logic or our convictions? I think there really should be some studies to see if we would reduce amputations. I think there are more problems that lead to the amputation than just dermatophytes.

Dr. Rich: Absolutely. I could not agree more.

Dr. Jennings: I have one last concern. I work at a large foot clinic, where we have 60,000 patient visits per year and that number is growing. Most of our population is African-American and there is a high incidence of diabetes within the female portion of that population. One of the problems we see with these diabetic patients is polypharmacy for hypertension and other conditions. My patients look at me and say, “If I’ve had this fungus for 20 or 30 years, why do you want me to take another drug?” Compliance becomes a major issue with patients who have diabetes. I wonder whether anyone has any pearls of wisdom on how to deal with these compliance issues.

Dr. Rich: That is a good point, and I do not know the answer.