Subclinical onychomycosis in patients with type II diabetes

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Abstract

Fungal organisms could be present in the nail without any clinical manifestations. As onychomycosis in diabetics has more serious complications, early detection of such infection could be helpful to prevent them. We aim in this study to assess the possibility of detecting subclinical onychomycosis in type II diabetic patients and addressing possible associated neuropathy. A cross sectional, observational study included patients with type II diabetes with normal big toe nail. All were subjected to nail clipping of the big toe nail, followed by staining with Hematoxylin and Eosin and Periodic-Acid-Schiff (PAS) stains and examined microscopically. A total of 106 patients were included, fungal infection was identified in eight specimens, all were uncontrolled diabetes, and six had neuropathy. Using the nail clipping and microscopic examination with PAS stain to detect such subclinical infection could be an applicable screening test for diabetic patients, for early detection and management of onychomycosis.

Introduction

Reports about fungi that could be present in the nail without any clinical manifestations have been documented,[1-4] and this was referred to as *Subclinical onychomycosis.*[3] Evidence that these fungi could change from the passive form to induce superficial fungal infection in case there is defect in the immune system of the patient was reported.[5]

Onychomycosis is a well known complication of diabetes mellitus. About one third of diabetic patients are affected.[6] Although onychomycosis doesn't represent a serious infection in most people, its risk is increased in diabetics, due to its limb threatening infection that could progress to ulcers and amputation as a result of the comorbidities present in diabetics, namely peripheral neuropathy, macro and microvascular diseases and impaired immunity in addition to foot deformities,[7] and thus it is critical to manage onychomycosis properly in such patients.

The approach to diagnose onychomycosis could be painful, prolonged and complicated. Nail clipping is an easy doing procedure, painless, cheap and reasonable.[8]

Accordingly, the aim of our study was to investigate the presence of subclinical onychomycosis in diabetic patients using nail clipping as a diagnostic tool, and addressing possible association of neuropathy with the occurrence of subclinical infection.

Materials and Methods

A cross sectional, observational study included participants with type II diabetes mellitus following up in endocrinology clinics presented to the clinic by issues unrelated to onychomycosis. Patients with any clinical nail dystrophy including discoloration, subungual debris, thickening, onycholysis, or patients with previous diagnosis of onychomycosis at least one year before the study were excluded.

Age, sex and history of associated medical condition, diabetes related factors including type of diabetes, duration, associated peripheral neuropathic symptoms (numbness, burning, tingling or loss of sensation) were recorded. Diabetic neuropathy was tested by testing the vibratory sensation by using a 128 Hz tuning fork on the interphalangeal joint of the right hallux comparing it to the dorsal wrist. Patients with lost vibration sense on the dorsal foot or feel stronger vibration on the wrist were considered having diabetic neuropathy. This method of detection of neuropathy was chosen due to its utility in clinical practice being simple and reliable.[9]

Heamoglobin A1c (HbA1c) was assessed for every patient; HbA1c level below 7.0% was considered as controlled diabetic patients.[10]

Nail clipping was done from a normal big toenail for each patient. The clippings were subjected for Hematoxylin and Eosin stain (H&E) and Periodic-Acid-Schiff (PAS) staining according to standard protocol.

The histopathologic criteria to diagnose onychomycosis included the presence of parakeratosis, serous lakes, hyperkeratosis and inflammatory cells (neutrophils) that may suggest the possibility of onychomycosis in H&E stained specimens and the presence of hyphae invading the plate in PAS stained sections.

A total of 106 patients with type II diabetes were included in the current study, 20 males (18.9%), and 86 females (81.1%). The duration of diabetes ranged from 2 months to 20 years with mean duration (7.9) years. The patients' age ranged from 25 to 75 years and a mean age

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Table 1. Factors associated with patients found to be positive for subclinical onychomycosis.

Factors, variables patients	Total patients	Patients with subclinical onychomycosis	Percentage of these within same group
Disease duration			
More than 10 years	42	5	7.8
Less than 10 years	64	3	7.1
Glycemic control			
Controlled	7	0	0
Uncontrolled	99	8	8.1
Neuropathy			
Present	48	6	12.5
Absent	58	2	3.4

Table 2. Previous studies reporting fungal infection in apparently normal nail.

Authors	Patients included	Patients with subclinical infection	Method used to diagnose fungal infection	Associated findings
Davis[1]	1954	170 (8.7%)	Direct microscopy (KOH) or culture	Active onychomycosis in other toenails
Baran and Badillet[2]	46 with normal toenails from total of 113 with onycholysis	7 (15%)	KOH, PAS staining where appropriate; fungal culture	Established T. rubrum toenail infection
Baran and Badillet[2]	52	2 (4%)	KOH, PAS staining where appropriate; fungal culture	None
Walling[3]	101	7 (1.5%) out of 66 6 out of 35 (17%)	Nail clipping with PAS staining	None Confirmed tinea pedis
Shemer *et al.*[4]	585	54 (9.2%) 23 (3.9%) 18 (3.1%)	KOH Culture KOH and culture	None None None
Our study	106	8 (7.5%)	Nail clipping with PAS staining	Diabetes mellitus type II

51.2 (±9.2) years, 49 patients were less than 50 years. 99 patients were uncontrolled diabetes (HbAlc 7) (93.4%), while the controlled were seven patients (6.6%). 43 patients were on oral hypoglycemic drugs (40.6%), and 63 were on insulin therapy (59.4%). Forty eight patients had neuropathy (45.30%) as revealed by absence or weak vibration sense using the tuning fork test. PAS stained specimens revealed eight cases positive for fungal infection, in which uniform septate hyphae were found. This accounts 7.5% of the total patients. These PAS positive eight cases were five females and three males, with age ranged from 40 to 70 with mean age 51.6 (±8.7). Four patients were on oral hypoglycemic drugs (9.3% of patients on oral hypoglycemic drugs), and the other four patients were on Insulin (6.3% of patients taking Insulin). Factors that were found to be associated with patients with subclinical onychomycosis are demonstrated in Table 1. Although follow up was not intended in our study, we found that five out of the eight patients had associated tinea pedis and two patients developed clinical onychomycosis after two and three months respectively during their visit to dermatology clinic.

Discussion and Conclusions

The microscopic findings were not correlated with culture, as the objective of this study was to search for subclinical infection in diabetics, and addressing associated possible risk factors for it, regardless of the causative agent, and using the most accurate method reported in the literature (finding hyphae in PAS stained specimens obtained by nail clipping). Larger population of type II diabetic patients is needed to be investigated in further studies in order to answer the question: *do we need to recommend screening diabetics for subclinical onychomycosis using nail clipping as a diagnostic tool in their routine checkup?*

Scant data about subclinical onychomycosis were reported (Table 2) and might be a finding in a percent of type II diabetic patients especially the uncontrolled ones which can be associated with tinea pedis and neuropathy. Using the nail clipping and microscopic examination with PAS stain to detect such subclinical infection could be an applicable screening test for diabetic patients, being non painful, reasonable, and simple test, aiming for early detection and management of onychomycosis and hence decreasing the incidence of its possible serious complications in diabetics and perhaps the serious side effects of prolonged systemic antifungal treatment.

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