Distribution of toenail dystrophy predicts histologic diagnosis of onychomycosis

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Background: Onychomycosis (OM) affects up to 10% of the general population and is associated with functional impairment. Clinically, OM can mimic nail psoriasis, trauma, lichen planus, oncyhogryphosis, and other disorders. Laboratory methods for diagnosing OM vary in accuracy and predictive value. Clinical clues to OM would help guide laboratory testing and decrease improper empiric antifungal therapy.

Objective: The goal of this study was to determine whether particular distribution patterns of toenail dystrophy are associated with fungal infection of the nail.

Methods: We retrospectively reviewed toenail clippings submitted over a 5-year period to our pathology department for periodic acid—Schiff (PAS) staining for diagnosis of OM.

Results: Specimens from a total of 311 patients (130 men, 181 women; mean age: 48.3 yrs; range: 19-97 yrs) were included. Overall, 150 specimens (48.2%) were histologically positive for OM. OM was significantly more likely to be diagnosed in men ($P < .01$), in persons over the age of 64 ($P < .02$), and in the context of tinea pedis ($P < .001$). Involvement of the third (41/65; 63.1%) or fifth (27/41; 65.9%) toenails of either foot significantly correlated with OM ($P < .025$). Dystrophy of the great toenail was seen in 257/311 (82.6%) and was associated with OM in about half of cases (128/257; 49.8%). Dystrophy of first and fifth nails on the same foot was predictive of OM (23/32; $P < .01$). Unilateral dystrophy correlated positively with OM (79/142; 55.6%; $P < .02$), with a stronger correlation when 2 or more nails were dystrophic (33/42; $P < .001$). Dystrophy of the second or fourth nails, a single nail, or all 10 nails did not support or contradict of OM. Female gender was a negative predictor for OM ($P < .001$).

Limitations: Potassium hydroxide and culture results were not available to correlate with histology. PAS staining of nail clippings has inherent diagnostic limitations.

Conclusions: Dystrophy of the third or fifth toenails, of the first and fifth nails on the same foot, unilateral dystrophy, male gender, an age over 64, and the presence of tinea pedis are all independent predictive factors of OM. Presence of these patterns of dystrophy may help to clinically distinguish OM and guide laboratory testing. (J Am Acad Dermatol 2007;56:945-8.)

Onychomycosis (OM) is a common problem, accounting for up to half of all diseases of the nail, with an estimated prevalence of 10% of the general population and approaching 60% in the elderly.[1-4] OM, generally caused by dermatophyte fungi, is often symptomatic and can cause functional impairment.[1] Previous studies have shown a correlation between OM and increasing age, psoriasis, tinea pedis, diabetes, peripheral arterial disease, malignancy, and immune dysfunction.[5-7] The clinical presentation of OM often involves hyperkeratosis with thickening and discoloration of the nail plate, though other disorders, such as nail psoriasis, onychogryphosis, lichen planus, nail trauma, local tumors, and vascular disorders, may yield a nearly identical clinical picture.[1,4] Methods of diagnosing OM include potassium hydroxide (KOH) microscopy, culture, and nail clipping with periodic acid—Schiff (PAS) staining for histologic exam. These methodologies vary in their accuracy, predictive value, and expense.[8,9] An accurate diagnosis of OM is important because systemic antifungal therapy is

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often indicated, which carries an additional expense and is occasionally associated with adverse events and drug interactions.[10,11] Moreover, empiric treatment of dystrophic nails with antifungal medication results in needless expense and risk.

We were interested in studying the pattern of toenail dystrophy in adult patients in whom OM was clinically suspected. The goal of this study was to determine whether particular distribution patterns of dystrophy were associated with an increased likelihood of fungal infection of the nail. We also studied the impact of demographic factors, such as age and gender, as well as commonly associated dermatoses, such as psoriasis and tinea pedis.

METHODS

After obtaining institutional review board approval, the Department of Pathology electronic databank was searched for instances of toenail clippings submitted within the 5-year period between January 1, 1999 and December 31, 2004 for PAS and histological examination. This method is the routine diagnostic test performed at our institution during this time period; cultures and KOH preparations are generally performed to supplement this data. All nail clippings included were obtained from adult patients for the purpose of determining the presence or absence of OM. Cases of nondermatophyte fungus (including presumed *Candida* species and molds; N = 6) were excluded. Demographic and clinical information was collected from this databank as well as from the electronic medical records of the associated clinic visit at which the nail plate biopsy was performed. Specimens for which a description of the distribution of nail dystrophy (described in terms such as thickening, discoloration, subungual hyperkeratosis, or debris) was unavailable were excluded. Repeated nail plate biopsies from the same patient were excluded, as were patients with previously documented treatment with systemic antifungal agents. The submitted clipping(s) from each patient included one or more affected toenails. Statistical analysis including chi-square analysis for qualitative variables and odds-ratio determination was performed by standard methods; $P < .05$ was considered statistically significant.

RESULTS

Specimens from a total of 311 patients (130 men, 181 women; mean age 48.3 yrs, range 19-97 yrs) were available for analysis. Overall, 150 specimens (48.2%) were histologically positive for OM (Table I). OM was significantly ($P < .001$) more likely to be diagnosed in men (78/130 specimens; 60%) compared to women (72/181 specimens; 39.8%), and in persons over the age of 64 (27/41 specimens; 65.9%; $P < .02$). The presence of tinea pedis was also positively correlated with OM ($P < .001$). When the clinical distribution of nail dystrophy was studied with the histologic results, involvement of the third or fifth toenails of either foot (with or without dystrophy of other nails) was significantly ($P < .025$) correlated with the presence of dermatophyte. Specifically, 41 of 65 (63.1%) cases involving the third toenail and 27 of 41 (65.9%) cases involving the fifth toenail were histologically positive for OM (Table I). Dystrophy of the great toenail was seen in 257 of 311 (82.6%) of cases, was associated with OM in about half of these (128/257; 49.8%), and was less likely to be associated with OM when both great toenails were dystrophic (25/56; 44.6%). Dystrophy of the first and fifth nails on the same foot (regardless of findings on the contralateral foot) was predictive of OM (23/32; $P < .01$). Involvement of the second or fourth toes did not support or contradict a diagnosis of OM, nor did involvement of a single toenail (46/101; 45.5%) or all toenails (24/45; 53.3%). Unilateral toenail dystrophy correlated positively with OM, with 79 of 142 (55.6%) positive ($P < .02$), and this correlation had a higher predictive value when two or more nails were dystrophic on the same foot (33/42; $P < .001$). Bilateral toenail dystrophy argued against OM with 43 of 100 (43%) positive. Female gender was the only negative predictor of OM ($P < .001$).

DISCUSSION

OM is a common disorder associated with significant morbidity and health care expense. Though most health care providers are familiar with the appearance of onychomycotic nails, surprisingly little data is available regarding the distribution patterns of dystrophy on individual patients. Moreover, patients may occasionally be treated unnecessarily with oral antifungal agents based on an erroneous clinical diagnosis without further diagnostic testing. Indeed, our study shows that less than half of clinically suspected toenails harbored histologically identifiable fungus, which is supported by other studies.[2,9] Observation of patterns of dystrophy particularly correlated with OM may serve to limit misdiagnosis and lead to appropriate clinical decision-making.

In this study, we found that dystrophy of the third or fifth toenails, dystrophy of the first and fifth nails on the same foot, and unilateral dystrophy, as well as male gender and age over 64, are predictive of a histologic diagnosis of OM. Female gender was a negative predictor. The presence of these patterns of dystrophy may help to clinically distinguish OM from mimickers such as psoriasis and nail trauma. The