

Proximal Subungual Onychomycosis in the Immunocompetent: A Case Report and Review of the Literature

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ABSTRACT

Proximal subungual onychomycosis (PSO), which predominantly involves the nail plate from the proximal nail fold, is the rarest form of onychomycosis. Classically associated with an immunocompromised state, PSO is an uncommon diagnosis in individuals without immunodeficiency. We present a case of a healthy 51-year-old man, who presented with a three-month history of white discoloration of multiple toenails. Physical examination revealed white, opaque patches on the proximal third nail plates of multiple toenails. The affected digits also demonstrated proximal onycholysis, subungual debris, and mild paronychia. Laboratory examinations, including routine serologic studies as well as human immunodeficiency virus and antinuclear antibodies, were within normal limits. Proximal nail fragments of the left hallux showed sections of dystrophic nail plate with mounds of parakeratosis, collections of neutrophils, and hyphae that highlighted with periodic acid-Schiff staining. The patient was diagnosed with PSO and tinea pedis bilaterally and treated with oral fluconazole with gradual improvement. This case of PSO highlights the potential for its rare occurrence in a healthy host. However, the clinical presentation of PSO should trigger an evaluation for possible immunodeficiency.

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INTRODUCTION

Onychomycosis, infection of the nail by fungus, is the most common nail disease.[1] Since the original classification in 1972, onychomycosis has been divided into clinical variants according to the pattern of nail involvement by site and mode of invasion.[1] Subtypes include distal lateral subungual (DLSO), white superficial, proximal subungual (PSO), endonyx, and total dystrophic onychomycosis.[1]

PSO, predominantly involving the nail plate from the proximal nail fold,[1] is the rarest form of onychomycosis, occurring in less than one percent of cases.[2,3] Classically associated with an immunocompromised state, PSO is uncommon in individuals without immunodeficiency.[4]

CASE REPORT

A healthy 51-year-old man presented with a three-month history of discoloration of multiple toenails. He reported white discoloration of his left hallux followed by similar changes of his left third toe and right hallux, second, and fourth toenails. Discoloration began at the proximal edge of the nail plate and extended distally over three months. The patient denied prior trauma and treatment. He reported discomfort while wearing closed-toe shoes, however denied any constitutional symptoms. A review of systems was otherwise negative. His medical history was significant for hypothyroidism treated with levothyroxine.

On physical examination, he was a well-appearing Caucasian male with findings notable for white, opaque patches on the proximal third nail plates of the left hallux and third toe and the right hallux, second, and fourth toenails (Figures 1 and 2). The affected digits demonstrated proximal onycholysis and subungual debris. Distal nail plates were uninvolved. There was mild erythema of the periungual skin of the affected digits, with marked edema of the left fifth nail subunit (Figure 1). Both feet featured interdigital scale and maceration (Figure 3), as well as plantar scale and erythema. Laboratory examinations, including routine serologic studies as well as human immunodeficiency virus (HIV) and antinuclear antibodies, were within normal limits. Proximal nail fragments of the left hallux showed sections of dystrophic nail plate with mounds of parakeratosis, collections of neutrophils, and hyphae that highlighted with periodic acid-Schiff (PAS) staining.

The patient was diagnosed with PSO and tinea pedis bilaterally. For ease of administration and favorable side effect profile, he was treated with oral fluconazole 200 mg daily for 4 weeks followed by fluconazole 400 mg weekly for 3 months with gradual improvement.

DISCUSSION

PSO, the rarest form of onychomycosis, is most commonly caused by *Trichophyton rubrum*, but other dermatophytes as well as non-dermatophytic molds (NDMs) and yeast have also been identified.[1,3,5] In the classic description of PSO, fungi initially invade the stratum corneum of the proximal nail fold to establish infection. Subsequently, fungi invade the nail

FIGURE 1. PSO of the left hallux and third toe with marked erythema and edema of the left fifth nail subunit.

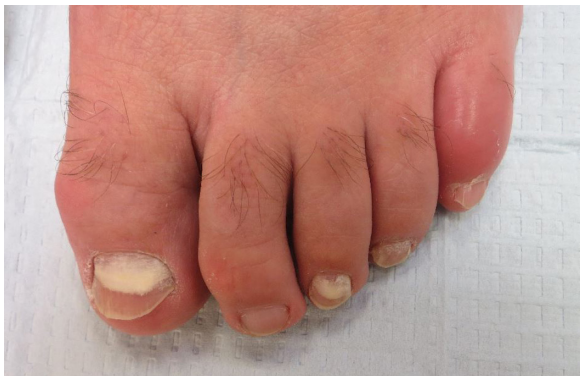


FIGURE 2. PSO of the right hallux, second, and fourth toenails.

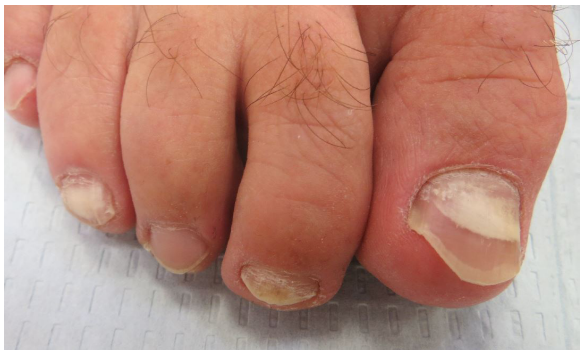
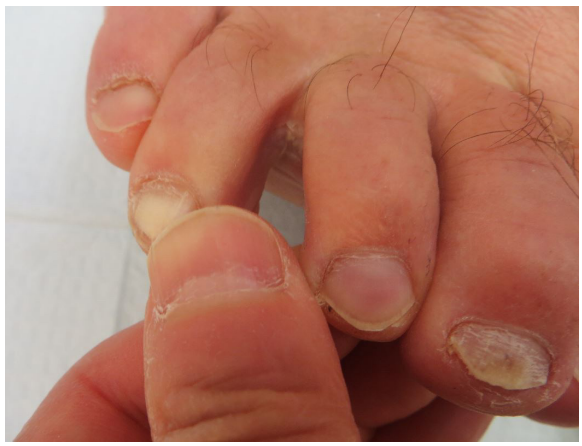


FIGURE 3. Interdigital scale and maceration between the right third and fourth toes



matrix and deeper portions of the ventral nail plate.[3] As the nail plate grows, the infection extends distally.[1] Invasion of the proximal nail plate may also occur secondary to paronychia, hematogenous, or lymphatic spread.[1] Regardless of the route of infection, fungi must achieve access to the proximal nail matrix for PSO to manifest.[3]

PSO is considered a sign of immunodeficiency and occurs, almost exclusively, in immunocompromised individuals.[2-4,6] The incidence of PSO in the immunocompetent population is 0.3% while that in the HIV+ population is almost 15 times greater at 4.2–5.0%.[2] In immunocompromised individuals, infection with dermatophytes has been found to be the most common cause[2,4], as HIV/AIDS appears to diminish resistance to the traditional pathogens that cause onychomycosis.[2] Consequently, PSO may be an indication for an evaluation for primary or secondary immunodeficiency.

PSO is most frequently found on the toenails but may involve the fingernails as well.[3] Infection presents as leukonychia or opaque, beige-white discoloration of the proximal nail plate.[4] Discoloration spreads distally from the lunula as the nail plate grows and may be associated with subungual hyperkeratosis, proximal onycholysis, and nail plate destruction.[3,6] Unlike other instances of onychomycosis, concomitant tinea pedis is uncommon.[3]

Diagnosis is confirmed with samples of the proximal ventral nail plate. To obtain a proper sample, the nail plate should be pared down to access the ventral side.[6] Samples should be prepared with potassium hydroxide, which will reveal hyphae under light microscopy, or examined histopathologically with PAS staining, the gold standard for diagnosing fungal onychomycosis.[3,6-8] In cases in which sufficient sampling is not possible via non-invasive means, punch biopsy of the nail plate may be considered. Mycological culture on agar without cycloheximide can identify the provocative organism.[6]

PSO is challenging to treat and requires systemic therapy following standard guidelines for onychomycosis.[1] A number of oral antifungal agents, including terbinafine[5,8], itraconazole[5], and fluconazole[6], as used in our patient (although not FDA-approved for the treatment of onychomycosis[6]), have been reported to be effective treatments. Occasionally combined therapy with oral and topical treatments with or without nail avulsion/surgery may be necessary.[1]

Our case of a 51-year-old man without immunodeficiency, who presented with PSO on multiple toenails, is unusual as PSO is rarely encountered in the immunocompetent.[4] Immunocompetent patients more frequently present with DLSO, the most common form of onychomycosis.[1,2] To our knowledge, there have been only a few reports of PSO occurring in immunocompetent patients (Table 1).[7-10] But within the limited available literature, NDMs are being increasingly considered as a cause of PSO, particularly in the immunocompetent. In a study of 431 patients with onychomycosis, NDMs were responsible for 13.6% of cases. More than half of those cases presented with PSO with only two associated with immunodeficiency.[5] Previously, NDMs were thought to be culture contaminants,

TABLE 1.

Clinical Data on Immunocompetent Patients With PSO Reported in the Literature

First Author (Year)	Patient Age & Sex	Etiologic Organism	Testing Performed	Treatment	Treatment Response
Piraccini (1996)[8]	36F	*Microsporum canis*	IgE 29 IU/dl, IgG 888 mg/dl, IgA 267mg/dl, IgM 118 mg/dl, total CD3+ 74%, CD4 45%, CD8 34%, CD4/CD8 ratio 1.32, CD3+ HLA-DR+ 8%, CD20 12%, CD20+ CD5+ 4%	Terbinafine 250mg PO daily x 2 months	Complete clinical and mycological cure
Baran (1997)[9]	1. 80F 2. 47F 3. 48M	All: *Fusarium* (*oxysporum*) species	Not documented	1. Nail avulsion with ciclopirox ointment and bifonazole ointment 2. Partial nail avulsion with 8% ciclopirox nail lacquer x 8 months 3. Not documented	1. Complete clinical and mycological cure 2. Complete clinical and mycological cure 3. Not documented
Weinberg (1999)[7]	1. 47F 2. 32F	1. *Fusarium* species 2. *Trichophyton rubrum*	1. HIV negative, CBC wnl 2. HIV negative, CBC & chemistry panels wnl	1. Itraconazole 200mg PO daily x 4 weeks 2. Itraconazole 200mg PO BID x 1 week/month x 2 months	1. Clinical improvement 2. Moderate clinical improvement
Schmidt (2015)[10]	44M	*Fusarium* species	HIV, hepatitis B, and hepatitis C negative	Terbinafine 250mg PO daily x 90 days	Complete clinical resolution

BID = twice a day, CBC = complete blood count, PO = orally, wnl = within normal limits.
*Tosti et al[5] also identified immunocompetent patients with PSO. Of the 59 cases of NDM onychomycosis reported in the study, 38 presented with PSO caused by either Scopulariopsis brevicaulis (10), *Fusarium* species (21), or *Aspergillus* species (7), and only 2 patients were immunocompromised. Clinical data were not available for the individual cases of PSO.

but further investigation has identified them as a noteworthy cause of PSO.[5,6] Our patient, although fungal culture was not obtained, demonstrated mild erythema and paronychia of his affected digits, suggesting his PSO may have been caused by a NDM. This would support the growing evidence demonstrating that NDMs can be an important cause of PSO in immunocompetent individuals.

PSO is an uncommon disease that is most frequently found in immunocompromised patients. Dermatophytes are the most common cause, while NDMs can also provoke the disease. This case of PSO highlights the potential for its rare occurrence in a healthy host. However, the clinical presentation of PSO should always trigger an evaluation for possible immunodeficiency illnesses.

DISCLOSURES

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