ONICHOMYCOSIS CAUSED BY ASPERGILLUS TERREUS

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Four cases of onychomycosis caused by *Aspergillus terreus* are presented. The clinical characteristics consisted of spotted and striated leuconychia, dark spots and fragility of the nails. The mycology is described, and it is shown that *A. terreus* has an inhibitory effect on the growth of dermatophytes and *Scopulariopsis brevicaulis*. Topical treatment with 1% Pimafucin in a mixture of 60% dimethylsulfoxide (DMSO) and 40% water as well as a 9% aqueous solution of sodium benzoate were both effective. The literature concerning onychomycosis caused by *A. terreus* is summarized.

Onychomycosis is a fungal infection of the nail plate. When fingernails are involved the causative fungi are dermatophytes and yeasts whereas dermatophytes and yeasts as well as molds may be isolated when toenails are involved. The most commonly isolated molds are various species of *Penicillinum*, *Aspergillus*, *Acremonium* and *Scopulariopsis*. Involvement of only one fingernail is often seen, whereas the involvement of several toenails is common. This is probably due to the heat and humidity around the toes (4).

*A. terreus* is a common saprophytic mold often found in soil and occasionally isolated from human skin and nails (5, 9, 11, 12). In *vitro* tests have shown that *A. terreus* is able to colonize hair (3, 7, 14).

CASE HISTORY

Patient no. 1 was a 40-year-old female who had been treated for arthrosis of the hip with injections of adrenocorticotropic hormones 20 years previous to our examination. A few months following these injections dark brown spots appeared on both great toenails. This discoloration spread to all the toenails. We found dark brown spots and circumscribed leuconychia of the nail plates of all toes. The nail plates were somewhat fragile but not thickened (Table 1, Fig 1). The surrounding skin was not involved, and the fingernails were normal. Direct microscopy and cultures of nail fragments were positive from all toenails as described under Materials and Methods. When the patient was made aware of the fungal cause of her discolored toenails she started treatment on her own with a 9% aqueous solution of sodium benzoate. This is occasionally used by laymen for the treatment of fungal diseases. After 2 weeks of treatment, microscopy and fungal cultures were negative, and the discolorations had faded. The nails had a normal appearance after 6 weeks of treatment.

Patients 2, 3 and 4 were all 70 years of age or older and they all presented nail changes consisting of discrete white spots and longitudinal stripes as well as dark brown spots on the distal parts of the nails (Table 1). The nail plates of the involved nails were fragile. For these patients microscopy as well as cultures from the involved nails were positive as described under Material and Methods. These patients were treated with 1% Pimafucin dissolved in a mixture of 60% DMSO and 40% water. Fungal cultures were negative after 6 weeks of treatment. At that time fungal elements
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Number of toenails involved</th>
<th>Clinical signs</th>
<th>Treatment</th>
<th>Other diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>female</td>
<td>10</td>
<td>Spotted leuconychia, dark spots, brittle nails</td>
<td>9% sodium benzoate</td>
<td>Arthritis of the left hip joint</td>
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<tr>
<td>2</td>
<td>75</td>
<td>male</td>
<td>2</td>
<td>Spotted leuconychia, dark spots</td>
<td>1% Pimacin in DMSO</td>
<td>Arteriosclerosis of the lower extremities</td>
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<tr>
<td>3</td>
<td>70</td>
<td>female</td>
<td>4</td>
<td>Striated leuconychia, dark spots, brittle nails</td>
<td>1% Pimafucin in DMSO</td>
<td>---</td>
</tr>
<tr>
<td>4</td>
<td>87</td>
<td>male</td>
<td>5</td>
<td>Dark spots</td>
<td>1% Pimafucin in DMSO</td>
<td>Bullous pemphigoid</td>
</tr>
</tbody>
</table>
could still be seen by microscopic examination. Clinically, no significant change was noted in the appearance of the nails.

MATERIALS AND METHODS

Nail fragments were examined microscopically after incubation for 1½ hours in 30% aqueous potassium hydroxide. Other nail fragments were cultured in Petri dishes at 26°C in Sabouraud’s peptone-glucose medium (1% neopeptone (Difco B119), 4% glucose and 2% agar) to which was added 40.000 IE streptomycin (Novo), 20.000 IE sodium-benzyl-penicillin (Novo) and 500 mg cycloheximide per liter medium.

Figure 1.—Toenails infected by Aspergillus terreus (patient no. 1 before treatment). Spotted dark brown discolorations and leuconychia are seen.

The colonies of A. terreus grew slowly on this medium. They were light brown with a whitish border; the reverse sides were grey-brown. An initially yellow pigment could be seen in the medium surrounding the colonies. Later it turned dark brown to black. The microscopic appearance of such colonies is thoroughly described by Raper & Fennel (11). Characteristically hyaline spores, 5 μm in diameter, were seen both in the direct microscopy of nail fragments (Fig. 2) and on the vegetative mycelium of the cultures. The following criteria were used to prove that A. terreus was the organism causing the nail changes: 1, In the direct microscopy the
mold was identified as an *Aspergillus* sp. by the hyaline spores and the presence of conidiophores. 2. The mold was isolated from the same site on 2 occasions with a one month interval. 3. A pure culture of *A. terreus* was obtained, and at least 10 colonies were seen for each of the patients presented here (Fig. 3). No dermatophytes or other pathogenic fungi were isolated.

Figure 2.—Direct microscopy of nail fragments in potassium hydroxide solution. x 400

An attempt was made to isolate bacteria from the nail fragments by culture on Sabouraud's peptone-glucose medium and 0.4% yeast extract (Difco). No pathogenic bacteria were isolated, but *A. terreus* colonies appeared also on this medium. Pigment production was, however, less pronounced.

Kaplan, Hooper and Heinemann (8) isolated dermatophyte-inhibiting terrein from *A. terreus*. We therefore attempted to determine whether this mold was antagonistic to various other nail-fungi. For these tests we used isolates of *Epidermophyton floccosum*, *Trichophyton mentagrophytes*, *Trichophyton mentagrophytes* var. *interdigitalis*, *Trichophyton rubrum* and *Scopulariopsis brevicaulis*. Two isolates of *A. terreus* were tested with each of the above mentioned fungi in Petri dishes using various agar media. Both isolates of *A. terreus* showed marked antagonism to all the other fungi; there was least antagonism to *Scopulariopsis brevicaulis* (Fig. 4).
Discussion

There are varying criteria for determining whether a fungus is pathogenic for nails (4, 14, 17, 19). We have included only those cases in which *A. terreus* was the only fungus isolated from clinically abnormal nails on 2 occasions with an interval of at least 1 month.

![Figure 3.—Appearance of culture of nail fragments after 14 days at 26°C showing numerous colonies of *Aspergillus terreus*.](image)

The mold was identified both by direct microscope examination and by culture. Deep distal onychomycosis is the most common clinical manifestation of onychomycosis. Superficial white onychomycosis appearing as white spots in the nail plate is also commonly seen. Less common manifestations are proximal onychomycosis and *Candida* onychomycosis (19). A diagnosis of onychomycosis cannot be made on clinical grounds alone but also requires both microscopy and culture (4).
The nail changes of the patient described in this report resembled superficial white onychomycosis. Except for the dark spots seen in our patients, this is in agreement with Zaias' description of nails infected with *A. terreus* (18). Another characteristic feature, which we also found, is fragility of the nails (2, 9, 10, 17, 18). None of our patients had involvement of the surrounding skin. This, too, is in agreement with the findings of other authors (5).

![Figure 4](https://example.com/figure4.jpg)

**Figure 4.**—Culture of both *Trichophyton mentagrophytes* and *Aspergillus terreus*, showing inhibited growth of *Trichophyton mentagrophytes*.

Three of our patients were 70 years of age or older. Decreased cell mediated immunity, poor circulation in the peripheral vessels, increased incidence of diabetes mellitus and senile nail changes found in older patients may account for frequent onychomycosis caused by molds in this age group (4, 13, 14, 16). Three of the patients in our study had or had previously suffered from serious diseases (Table 1).
Table 2.—Previously Reported Cases of Onychomycosis Caused by Aspergillus terreus

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number of patients</th>
<th>Age of patients</th>
<th>T toe-nails</th>
<th>F: finger-nails</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith, 1934</td>
<td>1</td>
<td>?</td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>Moore &amp; Weiss, 1948</td>
<td>1</td>
<td>47</td>
<td>T</td>
<td></td>
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<tr>
<td>Palderk &amp; Holmström, 1952</td>
<td>1</td>
<td>58</td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>Zaias, 1966</td>
<td>1</td>
<td>&gt; 50</td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>Walshe &amp; English, 1966</td>
<td>5</td>
<td>&gt; 40</td>
<td>4T, 1F</td>
<td></td>
</tr>
<tr>
<td>Botter, 1968</td>
<td>1</td>
<td>51</td>
<td>F</td>
<td></td>
</tr>
<tr>
<td>Blaschke-Hellmesen, 1968</td>
<td>1</td>
<td>?</td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>Schönbom &amp; Schmoranzer, 1970</td>
<td>1</td>
<td>75</td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>English &amp; Atkinson, 1973</td>
<td>3</td>
<td>&gt; 60</td>
<td>T</td>
<td></td>
</tr>
<tr>
<td>English &amp; Atkinson, 1974</td>
<td>16*</td>
<td>&gt; 60</td>
<td>T</td>
<td></td>
</tr>
</tbody>
</table>

*From one of these patients, Candida parapsilosis was isolated from the same nails.

Onychomycosis caused by *A. terreus* is probably more frequent than indicated by the figures in Table 2. English and Atkinson (6) found clinical changes consistent with onychomycosis among 168 of 216 consecutive patients in a chiropody clinic. Dermatophytes were isolated from nail fragments from 20 of the 168 patients; molds were isolated from 42 of these patients and yeasts from 13. *Aspergillus terreus* was only isolate from 15 patients with molds, and *A. terreus* as well as *Candida parapsilosis* were isolated from 1 other patient.

The discoloration seen in the nails of patients no. 1 disappeared more rapidly than could be explained by growth rate of the nails. This supports the assumption that the mold is located in the superficial part of the nail plate.

It is concluded that although *A. terreus* is infrequently described as the cause of onychomycosis, this condition is probably not uncommon, especially among older persons. Topical treatment with 1% Pimafucin in a mixture of 60% DMSO and 40% water, or 9% sodium benzoate were followed by negative fungal culture from the involved nails.

Zusammenfassung


References


