

CASE REPORT

DOUBLE-BLIND STUDY WITH TOPICAL ISOCONAZOLE AND TERBINAFINE FOR THE TREATMENT OF ONE PATIENT WITH BILATERAL *Tinea nigra plantaris* AND SUGGESTIONS FOR NEW DIFFERENTIAL DIAGNOSIS

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SUMMARY

The authors report a case of bilateral *Tinea nigra plantaris* treated through a double-blind study with the topical antifungal agents Isoconazole and Terbinafine. The objective of the study was to clinically compare the efficacy of these two topical antifungal agents on days 10, 20 and 30 of the treatment. No significant clinical differences were found, as all the plantar lesions regressed completely by the end of the treatment. Our conclusion was that in the case reported, the topical antifungal agents Isoconazole and Terbinafine demonstrated identical efficacy as a clinical cure. We also suggest the inclusion of injuries caused by arthropods of the Diplopoda Class in the differential diagnosis of *Tinea nigra plantaris*, due to the persistent acral hyperpigmentation.

KEYWORDS: Antifungal agents; Dermatomycoses; Mycoses; *Tinea*.

INTRODUCTION

Tinea nigra (TN) is a dermatomycosis caused by the fungus *Hortaea werneckii*^{4,8,9,10}. It is a cosmopolitan disease which is common in the coastal areas of tropical and subtropical regions^{2,3,4}. It generally affects young people below the age of 20 years, particularly females². Clinically, it manifests as a single, asymptomatic macule, ranging from dark brown to black in color, located on the palm of the hand. In rare instances it is bilateral^{2,3,4,11}. Sometimes it is located on the soles, or even in atypical areas^{1,2,3,4,8,12}. The differential diagnosis is made with melanocytic lesions and exogenous pigmentations^{2,3,6,11}.

The fungus is sensitive to treatment with various topical antifungal drugs^{4,6,8,9,10}. The objective of this communication, carried out as a double-blind study with Isoconazole and Terbinafine, was to clinically compare the efficacy of these two topical antifungal agents. The small number of reports of TN prompted the authors to carry out a review of cases with bilateral involvement published in Brazil. Additionally, we suggest the inclusion of injuries caused by arthropods of the Diplopoda Class in the differential diagnosis of *Tinea nigra plantaris*, due to the persistent acral hyperpigmentation.

CASE REPORT

Male patient, 19 years-old, student, living in Itajaí Town in Santa

Catarina State (SC), Brazil. Two years prior to the examination, he noticed the appearance of small, black, itchy spots on the plantar regions. He associated the spots with the fact that he had been walking barefoot on Cassino Beach in the state of Rio Grande do Sul, where he lived for six months. He reported no other symptoms, contact with insects or previous treatments.

On dermatological examination, the patient presented black macules with superficial fine peeling and irregular, poorly-defined edges. The macules ranged from 1 cm to 5 cm in diameter, and covered approximately two thirds of the plantar region (Fig. 1 and Fig. 2).

A direct mycological exam showed irregular, branching, septate, dematiaceous hyphae and the presence of yeast-like cells with spores (Fig. 3). Cultures were grown in Sabouraud agar medium on two separate occasions and once again before the treatment, with negative results.

Treatment was proposed with the topical antifungal agents Isoconazole and Terbinafine, through a double-blind study. The antifungal agents were poured separately into identical tubes by a pharmaceutical biochemist, with each tube containing the same amount of antifungal agent. The two tubes were labeled with the patient's name, the doctor's name, and the indication for topical use on the plantar regions - right or left. The topical treatments were applied by the patient twice a day for 30 days. The patient was clinically evaluated by the same dermatologist

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Fig. 1 - Black macules with fine desquamation and irregular, poorly-defined edges, ranging in size from 1 cm to 5 cm in diameter, covering approximately two thirds of the plantar regions.



Fig. 2 - Detail of the hyperchromic macules with fine desquamation, located on the left plantar region.

at days 10, 20 and 30 of the treatment. At the end of the treatment period, the professional responsible for the tubes revealed that the tube used on the right sole had contained Isoconazole, and the one used on the left sole had contained Terbinafine. All the lesions regressed and disappeared completely by the end of the treatment. No clinically significant differences were noted in the appearance of the regression of the lesions on the right and left plantar regions. The patient was followed up for 10 years, without any reappearance of the lesions.

DISCUSSION

Reports of TN in Brazil have been rare since the 1916 publication in Bahia by Cerqueira^{2,3,6,10,11}. The bibliographic review carried out for this

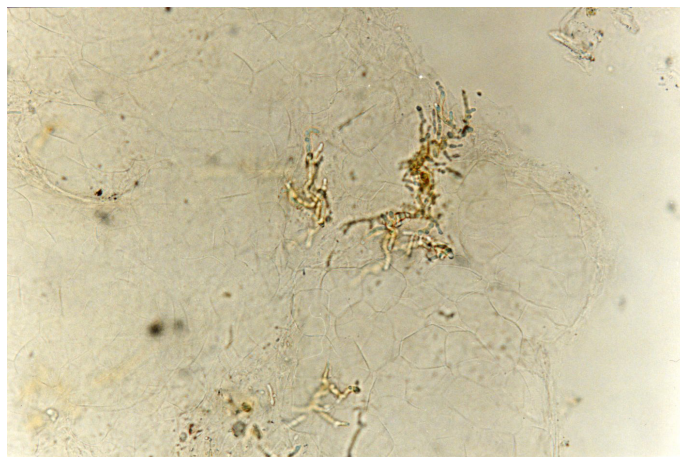


Fig. 3 - Direct, clarified mycological exam with 20% potassium hydroxide, showing irregular, branching, septate dematiaceous hyphae, and the presence of yeast-like cells with spores.

study found eight cases published in Brazil with bilateral involvement, shown in Table 1^{1,2,3,4,6,7,11,12}. Of these, there was only one case of bilateral plantar involvement, also in a young patient aged 19 years, but this time female². In the case of bilateral nail location¹², the presence of black spots was limited to the nails of the index fingers and left little beyond the hyperchromic macules on the right palmar area, the cultures of nail and scarce material were negative due to pretreatment performed by the patient, fact that made it impossible to claim certainty the diagnosis of TN. The nail lesions, despite the dematiaceous fungi, were probably not *Tinea nigra* but onychomycosis, due to non-dermatophyte fungi.

Since 1995, the authors have frequently observed TN on the north coast of Santa Catarina^{8,9,10}. During the 60th Congress of the SBD (Brazilian Dermatological Society) in 2005, twenty-seven cases were reported occurring over a 10-year period⁸. Recently, we described a case which evolved to a spontaneous cure and was confirmed by a mycological exam⁹, and two cases with curious forms analogous to formations in nature called “Heart” and “Parrot Beak”¹⁰.

The present case affects a male patient, the involvement is bilateral and the location of the lesions differs from the typical clinical manifestations of TN. The prolonged period of evolution before diagnosis may have contributed to the involvement of more extensive regions of the plantar areas than is usual.

We emphasize the importance of the differential diagnosis of melanocytic lesions, especially dysplastic nevi and malignant melanoma. The knowledge of dermatomycoses and dermoscopy may avoid surgical procedures in cases where melanocytic lesions lead to the misdiagnosis of TN. With pityriasis versicolor, the differentiation diagnostic occurs in the clinic according to the location, blackish color and usually absence of scaling lesions seen with TN. In our case we ruled out the diagnosis of fixed pigmented erythema. On top of the fact that the patient denied the use of systemic drugs, an increase in the size of the lesions was clinically observed once established. Cases of exogenous pigmentation blemishes varying from a shade of brown to a blackish color were due to impregnations by chemical dyes, grease or tar. Even though the patient had been walking barefoot in the sand, these cases were discarded because the spontaneous regression of such lesions occurs after several weeks of development.

Table 1
Bilateral *Tinea nigra*. Distribution of the epidemiological clinical data from eight cases published in Brazil from 1916 to 2011

Author(s), year of publication	Age	Sex	Place of residence: State	Squamation	Location
Silva & Mendonça ¹² 1932	11	F	Bahia	No	Ungueal
Aguiar ¹ 1937	38	F	Bahia	No	Palmar
Ramos e Silva ⁷ 1958	6	M	Rio de Janeiro	Yes	Palmar
Purim <i>et al.</i> ⁶ 1990	3	F	Paraná	No	Palmar
Gondim-Gonçalves <i>et al.</i> ³ 1991	9	F	Ceará	Yes	Palmar
Severo <i>et al.</i> ¹¹ 1994	5	M	Rio Grande do Sul	NR	Palmar
Giraldi <i>et al.</i> ² 2003	19	F	Paraná	No	Plantar
Larangeira Almeida <i>et al.</i> ⁴ 2007	5	M	Rio Grande do Sul	NR	Palmar

F - Female; M - Male; NR - No reported.

Apart from *Tinea pedis*, another differential diagnosis to be remembered in this case is the injuries caused by arthropods of the Diplopoda Class. Commonly known as millipedes, they release quinones and other irritative and pigmentary substances when threatened or crushed⁵. When the liquids and vapors expelled come into contact with human skin, they cause a burning sensation⁵. The site of contact instantly becomes hyperchromic, ranging in color from light yellow to dark brown, and lasting up to several months (Fig. 4). In the present case, the persistence of hyperpigmentation of the cutaneous lesions, with evolution of two years, which is considered prolonged; itching as the only symptom described; the absence of a sensation of burning in the plantar regions, and the lack of reported contact with insects; rules out a clinical diagnosis of accidents by arthropods. However, the persistent hyperpigmentation in accidents caused by Diplopoda in the plantar regions may be included as part of the differential diagnosis with plantar TN.



Fig. 4 - Detail of an area of black-colored exogenous pigmentation on the plantar region of the hallux, caused by a millipede inside his shoe in an accident that occurred as a child, simulating the clinical diagnosis of *Tinea nigra plantaris*.

As for the differential diagnosis cited, the presence of scaly lesions on the plantar regions may in this case suggest a hypothesis of *Tinea pedis*, which could be confirmed by a mycological exam. In the case reported

here, the culture was performed twice even with scaly lesions, both times with a negative result. On both occasions, the direct mycological exam revealed a finding of dematiaceous hyphae, reaffirming through laboratory tests the clinical diagnosis of TN.

In the treatment of bilateral TN, all the cases revised used various topical antifungal agents, always applying the same topical antifungal agent to all the cutaneous lesions^{1,2,3,4,6,7,11,12}. The treatment with topical Isoconazole and Terbinafine demonstrated the efficacy of both antifungal agents in the clinical cure of bilateral *Tinea nigra plantaris*, as well as enabling a comparative study of the efficacy of the two treatments in cases of bilateral *Tinea nigra*.

Although the study was limited and restricted to clinical evaluations during the physical examination, the medical literature reviewed did not find any reports of the use of the two topical antifungal agents, either simultaneously or separately, in the treatment of lesions with bilateral involvement of TN.

The authors conclude that future studies in cases of bilateral TN, whether plantar or palmar, as well as clinical evaluations, mycological exams and dermatoscopy, can be of use in making the comparative results of efficacy between various topical antifungal agents more quantifiable. Additionally, cases of bilateral TN must undergo a rigorous diagnostic process and new differential diagnoses of bilateral lesions are suggested in this communication.

RESUMO

Estudo duplo cego com Isoconazol e Terbinafina tópicos no tratamento de um paciente com *Tinea nigra plantaris* bilateral e sugestões para novos diagnósticos diferenciais

Os autores relatam um caso de *Tinea nigra plantaris* bilateral tratado através de um estudo duplo cego com os antifúngicos tópicos isoconazol e terbinafina. O objetivo do estudo foi comparar clinicamente a eficácia entre esses dois antifúngicos tópicos aos dias 10, 20 e 30 do tratamento, sendo que não foram observadas diferenças clínicas significativas, uma vez que todas as lesões plantares regrediram completamente no final do tratamento. Nossa conclusão foi que os antifúngicos tópicos isoconazol e terbinafina demonstraram a mesma eficácia na cura clínica do caso relatado. Adicionalmente, é sugerida a inclusão dos acidentes causados

por artrópodos da Classe Diplopoda no diagnóstico diferencial com a *Tinea nigra plantaris* devido a hiperpigmentação acral persistente.

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